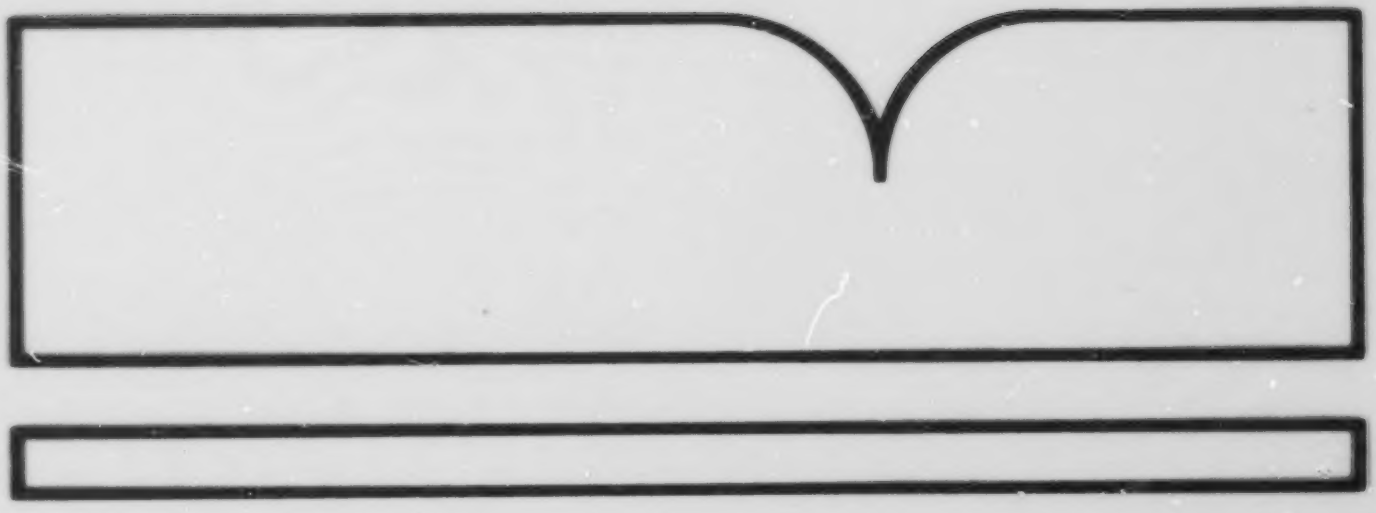
PB88-220744

Health and Environmental Effects Profile for Dimethylphenols

(U.S.) Environmental Protection Agency
Cincinnati, OH

Sep 86



U.S. Department of Commerce
National Technical Information Service
NTIS

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO. EPA/600/X-86/256	2. PB88-220744/AS
4. TITLE AND SUBTITLE Health and Environmental Effects Profile for Dimethylphenols	5. REPORT DATE September 1986
	6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO
9. PERFORMING ORGANIZATION NAME AND ADDRESS	10. PROGRAM ELEMENT NO.
	11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268	13. TYPE OF REPORT AND PERIOD COVERED
	14. SPONSORING AGENCY CODE EPA/600/22
15. SUPPLEMENTARY NOTES	

16. ABSTRACT The Health and Environmental Effects Profile for Dimethylphenols was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents. Quantitative estimates have been presented provided sufficient data are available. Dimethylphenols has been determined to be a systemic toxicant. Reference Doses (RfD), defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effect during a lifetime, for 2,6-dimethylphenol and 3,4-dimethylphenol are 0.042 and 0.098 mg/day, respectively, for oral exposure. The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. The RQ values for 2,6-dimethylphenol and 3,4-dimethylphenol are 100 and 1000, respectively. Existing data are insufficient to determine an RQ value for 2,3-, 2,4-, 2,5- and 3,5-dimethylphenol.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field Group

18. DISTRIBUTION STATEMENT Public	19. SECURITY CLASS (This Report) Unclassified	21. NO. OF PAGES 83
	20. SECURITY CLASS (This page) Unclassified	22. PRICE

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

PB88-220744

EPA/600/X-86/256
September 1986

HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR DIMETHYLPHENOLS

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
National Technical Information Service
SPRINGFIELD, VA. 22161

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1985.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic exposures. An RfD is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, RfDs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, DC.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Exposure Assessment Group
Reproductive Effects Assessment Group

Editorial review for the document series was provided by:
Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office, Cincinnati, OH

Technical support services for this document series were provided by:
Bette Zwayer, Pat Daunt, Karen Mann, and Jacky Bohanon
Environmental Criteria and Assessment Office, Cincinnati, OH.

EXECUTIVE SUMMARY

Dimethylphenols are isomeric phenolic compounds obtained by the substitution of two methyl groups in different ring positions of phenol. The six isomeric forms of dimethylphenols are 2,3-, 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dimethylphenol. All six isomers are white crystalline solids at ambient temperature (Weast, 1980). They are readily soluble in most organic solvents but slightly soluble in water (Windholz, 1983).

The dimethylphenols are very weak acids. They principally exist as nonionized protonated forms in surface waters. They are also susceptible to form chlorinated compounds that have lower taste and odor thresholds (OHMTADS, 1985).

Of the six possible isomers, only 2,6- and 3,5-dimethylphenol are commercially produced in the United States in recent years. Only two U.S. companies manufactured 2,6- and 3,5-dimethylphenol in 1984 (SRI, 1985; USITC, 1985). The mixed dimethylphenols were manufactured by two additional U.S. companies in 1984 (SRI, 1985). Data on the recent U.S. production volume for dimethylphenols is not available. The dimethylphenols are manufactured as a mixture from cresylic acid or tar acid fraction of coal tar (Hawley, 1981). Pure 2,6-dimethylphenol is commercially produced by the methylation of phenol (Reed, 1978).

The dimethylphenols are used as intermediates in the manufacture of antioxidants, pharmaceuticals, plastics and resins, disinfectant, solvent, insecticides and fungicides, rubber chemicals, wetting agents, dyestuffs, cresylic acid constituent, and polyphenylene oxide (2,6-isomer only) (Verschueren, 1983; Hawley, 1981).

In normal atmosphere, the most significant fate process for the removal of dimethylphenol is expected to be its reaction with the hydroxyl radical. The half-lives for these reactions have been estimated to be <6 hours. In polluted atmosphere, the reactions of nitrate radicals with the dimethylphenols are expected to be the fate determining processes. At a 355 ppt concentration of nitrate radicals as found in an air pollution episode in the Los Angeles basin (Carter et al., 1981), the half-lives of dimethylphenols that result from these reactions are expected to be a few minutes. The removal of atmospheric dimethylphenols through adsorption onto aerosol particles, dry deposition and wet deposition is expected to be insignificant.

The two nonphysical processes that are expected to be most significant in the removal of dimethylphenols from aquatic media are their reactions with peroxy radicals and biodegradation. From the estimated rate constant for 2,4-dimethylphenol reaction with peroxy radicals (Mabey et al., 1981), it has been estimated that the half-life for this reaction will be <1 day. There is some controversy regarding the significance of biodegradation in determining the fate of dimethylphenols in aquatic media. Biodegradation was found to be significant in natural water by some authors (Visser et al., 1977; Southworth et al., 1985), while Kaplin et al. (1968) reported that significant biodegradation of dimethylphenols is not likely. Based on the estimated biodegradation rate constant value given by Mabey et al. (1981), it is estimated that the biodegradation half-lives of dimethylphenols in natural water will be ~3 days. The loss of dimethylphenols from natural aquatic media through volatilization is likely to be insignificant. The

significance of the removal of these compounds through sorption onto suspended particles and sediments will depend on the nature of the particle. Sorption may become significant when the iron oxide or organic carbon content of the particles in aquatic media are high. Dimethylphenols are not expected to significantly bioconcentrate in aquatic organisms (Barrows et al., 1980; Davies and Dobbs, 1984).

The two processes that may determine the fate of dimethylphenols in soil are biodegradation and sorption (Humenick et al., 1982). Biodegradation, however, was found to be insignificant in the soil from a creosote waste disposal site (Goerlitz et al., 1985). The toxicity of chemicals towards the microorganisms may be responsible for the observed lack of biodegradability at this site. The sorption of dimethylphenols in soil will increase as the organic carbon and iron oxide content of the soil increases (Artiola-Fortuny and Fuller, 1982; Isaacson and Sawhney, 1984). Dimethylphenols may leach into groundwater because of the low sorption in sand aquifers (Goerlitz, et al., 1985). Should the number of microorganisms capable of degrading dimethylphenols decline, because of the presence of toxicants, then leaching would become the primary fate process in soil.

Although dimethylphenols have been identified in tobacco and marijuana smoke, exhaust from mobile and stationary sources, these compounds have never been reported to be present in ambient air. Hawthorne and Sievers (1984) failed to detect dimethylphenol in U.S. urban and rural air at a detection limit of 0.05 $\mu g/m^3$ for the individual compounds.

Dimethylphenols have been identified in the effluents from municipal wastewater treatment plants, petroleum industry discharges, secondary effluents from textile plants, effluents from coal liquefaction and gasification plants and oil shale treatment facilities. Of a total of 1304

effluent samples analyzed, 2% of the samples had detectable amounts of 2,4-dimethylphenol at a median concentration of <10 µg/ℓ (Staples et al., 1985). Only 0.1% of a total of 813 ambient water samples analyzed contained detectable levels of 2,4-dimethylphenol at a median concentration of <10 µg/ℓ (Staples et al., 1985). Dimethylphenols have been identified in groundwater near industrial operations and near waste dumpsites. The concentrations of 2,4- and 3,5-dimethylphenol at a depth of 6 m inside a wood preserving dumpsite in Florida were reported to be 5.65 and 9.52 mg/ℓ, respectively (Goerlitz et al,. 1985). With the exception of one reported instance (Shackelford and Keith, 1976), no isomer of diemthylphenol has ever been detected in U.S. drinking water.

Although dimethylphenols may be present in trace amounts in tea and in edible aquatic organisms from polluted waters, the quantitative level of the dimethylphenol in any food could not be located in the available literature as cited in the Appendix.

In terms of acute toxicity to fishes, 2,5-dimethlyphenol appears to be the most toxic of the dimethylphenol isomers, based on the few studies in which different isomers were compared. The 2,4-isomer is also relatively toxic. The lowest acutely toxic dimethylphenol concentration was 2 mg/ℓ 2,5-dimethylphenol, which was a 24-hour LC_{50} for rainbow trout embryos (Albersmeyer and von Erichsen, 1959). The only chronic toxicity data were provided by two fathead minnow embryo-larval tests, both of which indicated toxicity thresholds of 1-3 mg/ℓ (Holcombe et al., 1982; U.S. EPA, 1978). The limited information for aquatic plant species indicated that they were much less sensitive than fish or invertebrates. The only pharmacokinetic information available indicated that 2,4-dimethylphenol was not strongly bioaccumulated by bluegills (28-day BCF=150), and that elimination was rapid ($t_{1/2}$ = 1 day).

From the limited information available on 2,4- and 3,4-dimethylphenol, it appears that the dimethylphenols are extensively and rapidly absorbed from the gastrointestinal tract of rats (Miyamoto et al., 1969), rapidly distributed and eliminated from tissues, and rapidly metabolized to glucuronide and sulfate conjugates (Somani et al., 1981; Kaka et al., 1982). Urinary excretion accounted for ~94% of an oral dose in rats (Miyamoto et al., 1969). There was a tendency for 2,4-dimethylphenol to persist in the brain of rats after intravenous dosing (Somani et al., 1981).

No subchronic or chronic oral carcinogenicity studies have been performed on dimethylphenols. However, data are available to suggest that the 2,4-, 2,5-, 3,4- and 3,5-dimethylphenol isomers exhibit tumor-promoting activity on mouse skin. The 2,6-isomer was only weakly effective as a promoting agent (Boutwell and Bosch, 1959). All isomers except 2,6-methylphenol produced a small increase in carcinoma incidence when applied without an initiation.

The 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dimethylphenol isomers were found to be nonmutagenic when tested with or without metabolic activation in the TA98, TA100, TA1535, TA1537 and TA1538 strains of Salmonella typhimurium (Pool and Lin, 1982; Florin et al., 1980). The 2,4-isomer was negative in a reverse mutation assay using Escherichia coli Sd-4-73 (Szybalski, 1958).

Pertinent data regarding the teratogenicity and reproductive effects of dimethylphenols could not be located in the available literature as cited in the Appendix.

Studies concerning the chronic toxicity of methylphenols could not be located in the available literature. Limited information, however, was reported on the subchronic oral toxicity of 2,6- and 3,4-dimethylphenol.

No toxic effects were noted at 0.6 and 1.4 mg/kg when 2,6- and 3,4-dimethylphenol, respectively, were orally administered to white rats for 8 months (Veldre and Janes, 1979). At doses of 6 and 14 mg/kg (2,6- and 3,4-dimethylphenol) significant changes were noted in blood pressure and body weight, and histopathological changes were noted in the liver, kidney and spleen (Veldre and Janes, 1979; Maazik, 1967, 1970).

Provisional RfDs of 0.042 and 0.098 mg/day for 2,6- and 3,4-dimethylphenol, respectively, were derived based on the subchronic oral NOELs of 0.6 and 1.4 mg/kg/day in rats in the study by Veldre and Janes (1979). Uncertainty factors of 1000 were used. RQs of 100 and 1000 were derived for 2,6- and 3,4-dimethylphenol, respectively, based upon the liver and kidney pathology seen in rats at doses of 6 and 14 mg/kg/day, respectively, in the studies by Veldre and Janes (1979) and Maazik (1967).

Because of the limited evidence that the dimethylphenols act as promotors or whole carcinogens on the skin of mice (Boutwell and Bosch, 1959), these chemicals were placed in IARC Group 3 and CAG Group C (U.S. EPA, 1984b).

No toxic effects were noted at 0.6 and 1.4 mg/kg when 2,6- and 3,4-dimethylphenol, respectively, were orally administered to white rats for 8 months (Veldre and Janes, 1979). At doses of 6 and 14 mg/kg (2,6- and 3,4-dimethylphenol) significant changes were noted in blood pressure and body weight, and histopathological changes were noted in the liver, kidney and spleen (Veldre and Janes, 1979; Maazik, 1967, 1970).

Provisional RfDs of 0.042 and 0.098 mg/day for 2,6- and 3,4-dimethylphenol, respectively, were derived based on the subchronic oral NOELs of 0.6 and 1.4 mg/kg/day in rats in the study by Veldre and Janes (1979). Uncertainty factors of 1000 were used. RQs of 100 and 1000 were derived for 2,6- and 3,4-dimethylphenol, respectively, based upon the liver and kidney pathology seen in rats at doses of 6 and 14 mg/kg/day, respectively, in the studies by Veldre and Janes (1979) and Maazik (1967).

Because of the limited evidence that the dimethylphenols act as promotors or whole carcinogens on the skin of mice (Boutwell and Bosch, 1959), these chemicals were placed in IARC Group 3 and CAG Group C (U.S. EPA, 1984b).

TABLE OF CONTENTS

		Page
1.	INTRODUCTION	1
1.1.	STRUCTURE AND CAS NUMBER	1
1.2.	PHYSICAL AND CHEMICAL PROPERTIES	1
1.3.	PRODUCTION DATA	4
1.4.	USE DATA	5
1.5.	SUMMARY	5
2.	ENVIRONMENTAL FATE AND TRANSPORT PROCESSES	7
2.1.	AIR	7
2.2.	WATER	9
2.3.	SOIL	13
2.4.	SUMMARY	14
3.	EXPOSURE	17
3.1.	AIR	17
3.2.	WATER	18
3.3.	FOOD	21
3.4.	SUMMARY	21
4.	PHARMACOKINETCS	23
4.1.	ABSORPTION	23
4.2.	DISTRIBUTION	23
4.3.	METABOLISM	23
4.4.	EXCRETION	23
4.5.	SUMMARY	24
5.	EFFECTS	25
5.1.	CARCINOGENICITY	25
5.2.	MUTAGENICITY	26
5.3.	TERATOGENICITY	28
5.4.	OTHER REPRODUCTIVE EFFECTS	28
5.5.	CHRONIC AND SUBCHRONIC TOXICITY	28
5.6.	OTHER RELEVANT INFORMATION	29
5.7.	SUMMARY	31
6.	AQUATIC TOXICITY	33
6.1.	ACUTE	33
6.2.	CHRONIC	33
6.3.	PLANTS	36
6.4.	RESIDUES	36
6.5.	OTHER RELEVANT INFORMATION	38
6.6.	SUMMARY	38

TABLE OF CONTENTS (cont.)

	Page
7. EXISTING GUIDELINES AND STANDARDS	39
7.1. HUMAN	39
7.2. AQUATIC	39
8. RISK ASSESSMENT	40
9. REPORTABLE QUANTITIES	42
9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY	42
9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY	45
10. REFERENCES	49
APPENDIX: LITERATURE SEARCHED	66

LIST OF TABLES

No.	Title	Page
1-1	The Structures, Synonyms, Empirical Formulas and CAS Numbers for Dimethylphenols	2
1-2	Selected Physical Properties of the Six Isomeric Dimethylphenols	3
3-1	Concentration of 2,4-Dimethylphenol in Effluents and Ambient Water	20
5-1	Mutagenicity Testing of Dimethylphenols	27
5-2	LD_{50} Values of Dimethylphenols	30
6-1	Acute Toxicity of Dimethylphenols to Aquatic Organisms	34
6-2	Dimethylphenol Concentrations that Cause Chlorosis in Duckweed	37
9-1	Oral Toxicity Summary for Isomers of Dimethylphenol in Male Albino Rats	43
9-2	Oral Composite Scores for Isomers of Dimethylphenol in the Rat	44
9-3	2,6-Dimethylphenol: Mininimum Effective Dose (MED) and Reportable Quantity (RQ)	46
9-4	3,4-Dimethylphenol: Mininimum Effective Dose (MED) and Reportable Quantity (RQ)	47
9-5	2,3-, 2,4-, 2,5- and 3,5-Dimethylphenol: Mininimum Effective Dose (MED) and Reportable Quantity (RQ)	48

LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
CS	Composite score
DMBA	Dimethyl benzanthracene
EC_{50}	Concentration effective to 50% of recipients (and all other subscripted concentration levels)
i.p.	Intraperitoneal
i.v.	Intravenous
K_{oc}	Soil sorption coefficient standardized with respect to organic carbon
K_{ow}	Octanol/water partition coefficient
LC_{50}	Concentration lethal at 50% of recipients (and all other subscripted dose levels)
LD_{50}	Dose lethal to 50% of recipients
MATC	Maximum acceptable toxicant concentration
MED	Minimum effective dose
NOAEL	No-observed-adverse-effect level
NOEC	No-observed-effect concentration
NOEL	No-observed-effect level
ppb	Parts per billion
ppm	Parts per million
ppt	Parts per trillion
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Dimethylphenols are isomeric phenolic compounds obtained by the substitution of two methyl groups in the different ring positions of phenol. There are six isomeric forms of dimethylphenol. The structure, synonyms, empirical formula, molecular weight and CAS Registry numbers for these isomers are given in Table 1-1. Besides these individual compounds, a commercial mixture containing all the isomers is also available (Hawley, 1981).

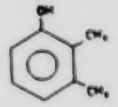
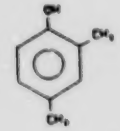
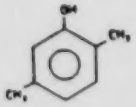
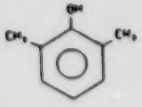
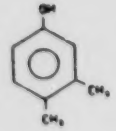
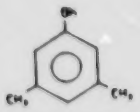
1.2. PHYSICAL AND CHEMICAL PROPERTIES

All six isomers of dimethylphenols are white, crystalline solids at ambient temperature (Weast, 1980). They are readily soluble in most organic solvents including ethanol, chloroform, ether and benzene. They are also soluble in sodium hydroxide solution (Windholz, 1983). Some of the physical properties of the six isomeric dimethylphenols are given in Table 1-2.

The dimethylphenols are very weak acids as indicated by their pK_a values given in Table 1-2. In surface waters, the dimethylphenols principally exist in their protonated, nonionized forms (OHMTADS, 1985). The compounds are susceptible to oxidation in air and the oxidation process is accelerated under alkaline conditions. This reaction, however, generally does not occur under environmental conditions (U.S. EPA, 1980). These compounds are easily chlorinated to form compounds with lower taste and odor thresholds (OHMTADS, 1985).

TABLE 1-1

The Structures, Synonyms, Empirical Formulas and CAS Numbers for Dimethylphenols

Structure	Synonyms[a]	Empirical Formula	Molecular Weight	CAS Registry Number[b]
	2,3-Dimethylphenol 2,3-Xylenol 1-Hydroxy-2,3-dimethylbenzene O-Xylenol 3-Hydroxy-O-xylene	$C_8H_{10}O$	122.16	526-75-0
	2,4-Dimethylphenol 2,4-Xylenol 1-Hydroxy-2,4-dimethylbenzene m-Xylenol 4-Hydroxy-1,3-dimethylbenzene 2,4-DMP	$C_8H_{10}O$	122.16	105-67-9
	2,5-Dimethylphenol 2,5-Xylenol 1-Hydroxy-2,5-dimethylbenzene p-Xylenol Hydroxy-p-xylene 2-Hydroxy-1,4-dimethylbenzene	$C_8H_{10}O$	122.16	95-87-4
	2,6-Dimethylphenol 2,6-Xylenol m-2-Xylenol 2-Hydroxy-m-xylene 1-Hydroxy-2,6-dimethylbenzene	$C_8H_{10}O$	122.16	576-26-1
	3,4-Dimethylphenol 3,4-Xylenol O-4-Xylenol 1-Hydroxy-3,4-dimethylbenzene 4-Hydroxy-1,2-dimethylbenzene 4,5-Dimethylphenol	$C_8H_{10}O$	122.16	95-65-8
	3,5-Dimethylphenol 3,5-Xylenol 1-Hydroxy-3,5-dimethylbenzene 1,3,5-Xylenol	$C_8H_{10}O$	122.16	108-68-9

[a]OHMTADS, 1985; CASR, 1985

[b]OHMTADS, 1985

0777p 05/08/86

TABLE 1-2

Selected Physical Properties of the Six Isomeric Dimethylphenols

Compound/Property	Isomer						Reference
	2,3-	2,4-	2,5-	2,6-	3,4-	3,5-	
Melting point, °C	75	27-28	75	49	66-68	68	Weast, 1980
Boiling point at 1 atm., °C	218	210	211.5	212	225	219.5(sublimes)	Weast, 1980
Density (g/cm³) at 20/4°C	1.5420	0.9650	0.971[a]	NA	0.9830	0.9680	Weast, 1980; Verschueren, 1983
Water solubility, mg/l	NA	7867 at 23°C 6474 at 20°C[b]	2050 at 23°C[c]	4406 at 20°C[b]	2876 at 23°C[c]	3627 at 20°C[b]	Banerjee et al., 1980; Rogers, 1982
Log K_{ow}	NA	2.30; 2.42; 2.50	2.33	2.36	2.23	2.35	Hansch and Leo, 1981; Westall et al., 1985; Garst and Wilson, 1984; Banerjee et al., 1980
Vapor pressure, mm Hg	0.005 at 10°C 0.075 at 20°C	0.02 at 9.9°C 0.075 at 20°C	0.005 at 9.6°C 0.075 at 20°C	0.02 at 4.9°C 0.15 at 20°C	0.002 at 10°C 0.075 at 20°C	0.003 at 9.7°C 0.075 at 20°C	Chao et al., 1983 Weber et al., 1981
PKa	10.4	10.4; 10.5	10.3; 10.2	10.6	10.4	10.1	Fujita and Nakajima, 1969; Pearce and Simkins, 1968
Henry's Law Constant, atm-m³/mol	NA	1.5x10⁻⁶[d]	5.9x10⁻⁶[d]	5.5x10⁻⁶[d] 6.6x10⁻⁶	4.2x10⁻⁶[d]	3.3x10⁻⁶[d]	Hawthorne et al., 1985
Air odor threshhold concentration, mg/m³	NA	0.001	2.0-2.3	0.0002	0.003	0.00004	Verschueren, 1983
Water odor threshhold concentration, mg/l	0.03	0.4	0.4	0.4	1.2	5.0	Verschueren, 1983

[a]The temperature at which the value was measured was not specified.

[b]These are aqueous solubilities in the presence of 0.15 M NaCl.

[c]These are values estimated from the correlation equation of Banerjee et al. (1980) by using the K_{ow} values given in the table.

[d]These are values estimated from the vapor pressure and solubility data given in the table.

NA = Not available

0777p

05/08/86

1.3. PRODUCTION DATA

According to the TSCA Inventory (U.S. EPA, 1977) the number of companies and the number of production sites that were involved in the production of the different isomeric dimethylphenols in 1977 were as follows:

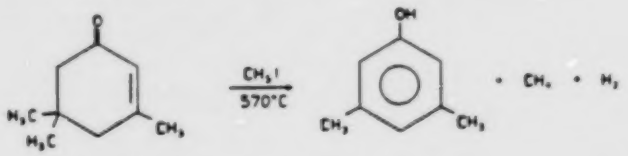
2,3-dimethylphenol, 4 companies at 4 locations
2,4-dimethylphenol, 5 companies at 5 locations
2,5-dimethylphenol, 5 companies at 5 locations
2,6-dimethylphenol, 6 companies at 6 locations
3,4-dimethylphenol, 5 companies at 5 locations
3,5-dimethylphenol, 4 companies at 4 locations

The Directory of Chemical Producers (SRI, 1985) lists the following companies as the U.S. producers of dimethylphenols as of January 1985:

2,6-dimethylphenol, General Electric Co., Selkirk, NY;
3,5-dimethylphenol, Ferro Corp., Santa Fe Springs, CA;
mixed dimethylphenols, Ferro Corp., Santa Fe Springs, CA and Stimson Lumber Co., Anacortes, WA.

The USITC (1985) lists the same two companies as the U.S. manufacturers of 2,6-dimethylphenol and 3,5-dimethylphenol at the end of 1984. Recent U.S. production volume for any isomers of dimethylphenol is unavailable.

Dimethylphenols are manufactured as a mixture from the distillation of cresylic acid or tar acid fraction of coal tar (Hawley, 1981). 2,6-Dimethylphenol, however, is commercially produced by another method; the methylation of phenol with methyl alcohol over a MgO or MgO-Fe_2O_3 catalyst at a temperature of 300-450°C selectively produces o-cresol and 2,6-dimethylphenol (Reed, 1978). 3,5-Dimethylphenol can be selectively manufactured by heating isophorone with methyl iodide at 570°C according to the following reaction (Papa and Sherman, 1981):



This method, however, is probably not used for the commercial production of 3,5-dimethylphenol.

1.4. USE DATA

The dimethylphenols are used as intermediates in the manufacture of antioxidants, pharmaceuticals, plastics and resins, disinfectants, solvents, insecticides and fungicides, rubber chemicals, wetting agents, dyestuffs and cresylic acid constituents (Verschueren, 1983). In addition, the 2,6-isomer is used in the manufacture of polyphenylene oxide (Hawley, 1981).

1.5. SUMMARY

Dimethylphenols are isomeric phenolic compounds obtained by the substitution of two methyl groups in different ring positions of phenol. The six isomeric forms of dimethylphenols are 2,3-, 2,4-, 2,5 , 2,6-, 3,4- and 3,5-dimethylphenol. All six isomers are white crystalline solids at ambient temperature (Weast, 1980). They are readily soluble in most organic solvents but slightly soluble in water (Windholz, 1983).

The dimethylphenols are very weak acids. They principally exist as nonionized protonated forms in surface waters. They are also susceptible to form chlorinated compounds that have lower taste and odor thresholds (OHMTADS, 1985).

Of the six possible isomers, only 2,6- and 3,5-dimethylphenol are commercially produced in the United States in recent years. Only two U.S. companies manufactured 2,6- and 3,5-dimethylphenol in 1984 (SRI, 1985; USITC, 1985). The mixed dimethylphenols were manufactured by two additional U.S. companies in 1984 (SRI, 1985). Data on the recent U.S. production volume for dimethylphenols is not available. The dimethylphenols are manufactured as a mixture from cresylic acid or tar acid fraction of coal tar (Hawley, 1981). Pure 2,6-dimethylphenol is commercially produced by the methylation of phenol (Reed, 1978).

The dimethylphenols are used as intermediates in the manufacture of antioxidants, pharmaceuticals, plastics and resins, disinfectant, solvent, insecticides and fungicides, rubber chemicals, wetting agents, dyestuffs, cresylic acid constituent, and polyphenylene oxide (2,6-isomer only) (Verschueren, 1983; Hawley, 1981).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. AIR

Sufficient information is not available to comprehensively evaluate the atmospheric fate of dimethylphenols. Qualitative estimation about some of their atmospheric behaviors can be made, however, by drawing analogies from the atmospheric fate of structurally similar compounds.

The rate constant for OH radical reaction with phenol at 23°C is 28.3×10^{-12} cm^3 $molecule^{-1}$ sec^{-1} (Atkinson, 1985). Assuming the atmospheric concentration of OH radicals as 10^6 molecule cm^{-3} (Cupitt, 1980), the half-life of phenol that results from this reaction is estimated to be ~7 hours. Introduction of an electron donating group, such as a methyl group is expected to increase the reactivity of the substituted phenol towards its reaction with OH radicals. In fact, from the experimental values of the range of reaction rate constant of 34.1×10^{-12} to 57.0×10^{-12} cm^3 $molecule^{-1}$ sec^{-1} (Atkinson, 1985), the half-life range of the isomeric cresols has been estimated to be ~3-6 hours. Substitution of a second methyl group is expected to increase the reaction rate even further than the rates with cresols. Therefore, the atmospheric reaction of dimethylphenols with OH radicals is expected to be one of the most significant fate determining processes. The half-lives for these reactions are expected to be <6 hours.

The rate constant for ozone reaction with phenol and cresols are estimated to be 1×10^{-18} cm^3 $molecule^{-1}$ sec^{-1} and 0.6×10^{-18} cm^3 $molecule^{-1}$ sec^{-1} (Cupitt, 1980). On the basis of atmospheric O_3 concentration of 10^{12} molecules cm^{-3} (Lyman et al., 1982), the corresponding estimated half-lives are 8 and 13 days. Therefore, it is concluded that the substitution of a methyl group to phenol has the effect of decreasing

its reaction rate with atmospheric O_3. The reaction of dimethylphenols with atmospheric O_3 is expected to be even slower and this reaction will not be a significant fate determining process.

In polluted atmosphere, nitrate radicals ($NO_3\cdot$) are formed from the reaction of O_3 with NO_2 (Carter et al., 1981):

$$O_3 + NO_2 \rightleftharpoons NO_3 + O_2$$

The rate constants for NO_3 radical reaction with phenol, o-cresol, m-cresol and p-cresol at 27°C are 2×10^{-12}, 12×10^{-12}, 7×10^{-12} and 13×10^{-12} cm^3 $molecule^{-1}$ sec^{-1}, respectively (Carter et al., 1981). During an air pollution episode in the Los Angeles basin, up to 355 ppt (8.9×10^9 molecule cm^{-3}) of NO_3 was detected ~1 hour after sunset (NO_3 photolysis is relatively rapid) (Carter et al., 1981). Under these conditions, the half-lives of phenol and o-, m- and p-cresols, which are due to their reaction with NO_3 radical, are <1 minute (Carter et al., 1981). Therefore, in polluted atmospheres this reaction can be a major sink for atmospheric phenol and cresols. Although no rate constants data are available for the reaction of dimethylphenols with NO_3 radicals, these reactions are expected to be major sinks in moderately to highly polluted atmospheres.

No data on direct photolysis of dimethylphenols in the atmosphere are available. The absorption spectra of 2,5-, 2,6- and 3,5-dimethylphenol in methanol solution show an absorption maximum at ~280 nm. The absorption at wavelengths >290 nm, however, are very weak (Sadler, n.d.). Therefore, direct photolysis of dimethylphenols is not likely to be a significant process.

The rates of physical removal processes for dimethylphenol from the atmosphere are not available. According to Cupitt (1980), the physical removal probability of o-, m- and p-cresol from the atmosphere is low.

Therefore, it is speculated by analogy that significant removal of atmospheric dimethylphenols will not occur through adsorption onto aerosol particles, dry deposition or wet deposition.

2.2. WATER

The vast majority of investigations on the fate of dimethylphenols in aquatic media is devoted to their ability to biodegrade. Considerable data gaps exist pertaining to the fate of dimethylphenols with respect to chemical reactions in aquatic media. Since dimethylphenols do not contain hydrolyzable functional groups, they are not expected to undergo hydrolysis in aquatic media (Mabey et al., 1981). The rate constants for singlet oxygen ($^1O_2$) and peroxy radical ($RO_2\cdot$) reactions with 2,4-dimethylphenol have been estimated to be $<4\times10^6$ and 1.1×10^8 M^{-1} hr^{-1}, respectively (Mabey et al., 1981). If the concentrations of $^1O_2$ and RO_2 radical in natural aquatic media are assumed to be 10^{-12} and 10^{-9} M, respectively (Mill et al., 1980), the reaction of 2,4-dimethylphenol with peroxy radicals will be significant. The half-life for this reaction is estimated to be 6.3 hours.

The reaction of chlorine on dimethylphenols may be significant since similar reactions may occur during chlorination of drinking water. The reaction of 2,6-dimethylphenol with aqueous chlorine dioxide at a molar ratio of chlorine dioxide/phenol of 1.3-1.7 was studied by Lindgren and Ericsson (1969). The main products of the reaction were 2,6-dimethyl-1,4-benzoquinone, 5,6-epoxy-2-hydroxy-cis-2,6-dimethylcyclohex-3-en-1-one, and 4-chloro-2,6-dimethylphenol. Unfortunately, the rate of this reaction was not reported. Studies on the direct photolysis of dimethylphenols in aquatic media have not been located in the available literature as cited in the Appendix. Although dimethylphenols do not have significant absorption

at wavelengths >290 nm (see Section 2.1.), they significantly absorb light of wavelengths >290 nm in basic solutions (Sadtler, n.d.). Therefore, it is likely that photoreaction will be significant in basic solutions, although no qualitative estimate of the half-life for this reaction can be given for the lack of reaction rate or quantum yield data.

The biodegradability of methylphenols has been studied by several authors with both pure cultures and mixed cultures. It was shown by Kramer and Doetsch (1950) that pure cultures of the genera Micrococcus, Vibrio and Achromabacter do not significantly utilize 2,6-dimethylphenol as sole carbon source. Several species of Pseudomonas, however, were shown to biodegrade dimethylphenols (Chapman and Hopper, 1968; Hopper and Chapman, 1971; Poh and Bayly, 1980). The pathway for this biodegradation is usually through alkyl-substituted hydrobenzoic acid and alkyl-substituted gentisic acids. The biodegradability of alkyl phenols with mixed microorganisms was studied by several investigators. With sewage as microbial inoculum, the degradation of 3,4- and 3,5-dimethylphenol was reported to be 57 and 31%, respectively, after 5 days of incubation (Heukelekian and Rand, 1955). With adapted activated sludge as microbial inoculum, the degradations of 2,3-, 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dimethylphenol after 5 days of incubation were reported to be 90% or better (Pitter and Kucharova-Rosolova, 1974; Pitter, 1976). On the other hand, Bridie et al. (1979a) reported only 4% biodegradation of 3,5-dimethylphenol after a 5-day incubation of the substrate in the presence of effluent from a sanitary waste treatment plant. The degradation of 2,4-dimethylphenol was reported to be almost complete in a 5-day incubation with settled domestic wastewater as microbial inoculum (Tabak et al., 1981). Tabak et al. (1981) reported that the degradation of 2,4-dimethylphenol was significant and the microorganisms were capable of rapid

adaptation in the presence of 2,4-dimethylphenol. Similarly, other authors have shown the biodegradability of dimethylphenols by phenol-adapted mixed microorganisms isolated from soils (Chambers et al., 1963; Tabak et al., 1964). Under the Japanese MITI test conditions, consisting of 100 ppm of test substance inoculated with 30 ppm activated sludge at 25°C for 2 weeks, 2,6-dimethylphenol was found to be biodegradable (Kitano, 1978). The removal of 2,4-dimethylphenol from industrial wastewater by the addition of powdered activated carbon to the biological removal (activated sludge) process was reported to be 90% (Dunn and Hutton, 1983). Patterson and Kodukala (1981) reported only >32% removal of 2,4-dimethylphenol from an industrial effluent treated with activated sludge.

The biodegradability of dimethylphenols in natural water has been studied by several authors. The degradation of dimethylphenols in a polluted part of the St. Lawrence River was attributed mainly to the action of phenol-utilizing microorganisms (Visser et al., 1977). Degradation was found to increase with the acclimation of microorganisms. The dimethylphenol degrading microorganisms were found to fluctuate with seasonal variation (Visser et al., 1977). Similarly, the environmental fate of dimethylphenols in coal-derived oil spilled intermittently on water was evaluated in aquatic microcosms (Southworth et al., 1985). The major process removing the dimethylphenols from the microcosms was biodegradation. Dimethylphenols disappeared within several weeks after acclimation of the microorganisms. The rate of removal of individual dimethylphenols was found to depend on microcosm exposure history and the presence of other phenol isomers (Southworth et al., 1985). Similar microcosm experiments performed by Kaplin et al. (1962) reported, however, that dimethylphenols degraded very slowly in natural water and significant biological degradation of dimethylphenol is not likely.

The biodegradation half-life for 2,4-dimethylphenol in natural water can be speculated from the estimated biotransformation rate constant of $1x10^{-7}$ mℓ $cell^{-1}$ $hour^{-1}$ (Mabey et al., 1981) and the concentration of microorganisms as 10^5 cells $mℓ^{-1}$ at 20°C (Visser et al., 1977). This produces a half-life of ~3 days for dimethylphenols in natural water. During winter months when the temperature of water is low, the concentration of phenolutilizing microorganisms may be $<10^3$ cell $mℓ^{-1}$ (Visser et al., 1977). Therefore, biodegradation may be very slow under such conditions. The biodegradability of dimethylphenols under anaerobic conditions was tested with domestic anaerobic sludge in Hungate serum bottles (Fedorak and Hrudey, 1984). It was reported that these compounds do not undergo anaerobic methanogenesis.

Few studies are available that can be used to predict the loss of dimethylphenols from aquatic media through physical processes. Loss through volatilization can be qualitatively predicted from the Henry's Law Constant (Lyman et al., 1982). The estimated Henry's Law Constant values for dimetnylphenols range from $1.5x10^{-6}$ to $5.9x10^{-6}$ atm·m^3/mol (see Table 1-2). Therefore, none of these compounds are expected to volatilize significantly from bodies of water. A pilot study conducted to determine the fate of dimethylphenols in various processes of wastewater treatment plants showed that a maximum of <1% of 2,4-dimethylphenol was removed through stripping (Petrasek et al., 1983). This study demonstrates that the loss of dimethylphenols through volatilization is likely to be insignificant. The removal of dimethylphenols through adsorption onto suspended particulate matter and sediments can be estimated from the equation, log K_{oc} = 0.544 log K_{ow} + 1.377 (Lyman et al., 1982). Since the log K_{ow} values for dimethylphenols range from 2.23-2.50 (see Table 1-2), K_{oc}

values may range from 390-550. Therefore, the dimethylphenols are expected to demonstrate weak sorption towards suspended particles and sediments in aquatic media and removal through this process may not be significant. The sorption of dimethylphenols, however, may not be due to interaction with neutral molecular species, but due instead to anionic interaction (Artiola-Fortuny and Fuller, 1982). In such cases, the presence of iron oxide was found to enhance sorption. Therefore, the increase in the percentage of iron oxide in the clay of suspended particles and sediments will enhance the sorption process to a point where it may become a significant removal mechanism.

The BCF for 2,4-dimethylphenol in the whole body of the bluegill sunfish, Lepomis macrochirus, under apparent equilibrium conditions, was experimentally determined to be 150 (Barrows et al., 1980; Davies and Dobbs, 1984). Assuming that the other dimethylphenols have similar BCFs, these compounds are not expected to bioconcentrate significantly in aquatic organisms.

2.3. SOIL

Sufficient information is not available in the literature to predict the fate of dimethylphenols in soils. Pertinent information on the possible chemical reactions of dimethylphenols in soil could not be located in the available literature as cited in the Appendix. Based on its photolytic behavior in aquatic media, photolysis of dimethylphenol on basic soil surfaces is possible; however, no quantitative estimate of the significance of this reaction in determining the overall fate of these compounds in soil can be given.

The biodegradability of dimethylphenols in soil has been investigated by a few authors. The reduction in the levels of dimethylphenols in ground-waters compared with the soil from an in situ underground coal gasification

plant was attributed partly to biodegradation of these compounds (Humenick et al., 1982). On the other hand, from the study of the concentrations of dimethylphenols in groundwater at different depths of the disposal site of a creosote plant in Florida, Goerlitz et al. (1985) concluded that dimethylphenols are not amenable to significant biodegradation in this sand aquifer.

Pertinent data on the volatilization of dimethylphenols from soil could not be located in the available literature as cited in the Appendix. Based on the volatility of these compounds in aquatic media (see Section 2.2.), it is predicted that significant loss of dimethylphenols through volatilization will not occur. The sorption of dimethylphenols by soil has been studied by several investigators. Isaacson and Sawhney (1984) studied the sorption of 2,6-dimethylphenol vapor on clay surfaces; the net sorption was ~3-4% of the equilibrium vapor weight. The sorption of aquatic dimethylphenols by soil were reported by Artiola-Fortuny and Fuller (1982). The adsorption constant varied from 262-5330, depending on the nature of the soil. A higher percentage of iron oxide and the intermediate pH of the soil were found to increase dimethylphenol adsorption. This study, however, was conducted with mineral soils with low levels of organic carbon (0.3-0.9%). Isaacson and Sawhney (1984) reported increased adsorption of 2,6-dimethylphenol with increases in organic carbon content of the soil. The significant sorption of dimethylphenol by an aquifer in an underground coal gasification site was reported by Humenick et al. (1982). A sand aquifer near a creosote disposal site, however, did not significantly adsorb the dimethylphenols, particularly 2,4- and 3,5-dimethylphenol (Goerlitz et al., 1985).

2.4. SUMMARY

In normal atmosphere, the most significant fate process for the removal of dimethylphenol is expected to be its reaction with the hydroxyl radical.

The half-lives for these reactions have been estimated to be <6 hours. In polluted atmosphere, the reactions of nitrate radicals with the dimethylphenols are expected to be the fate determining processes. At a 355 ppt concentration of nitrate radicals as found in an air pollution episode in the Los Angeles basin (Carter et al., 1981), the half-lives of dimethylphenols that results from these reactions are expected to be a few minutes. The removal of atmospheric dimethylphenols through adsorption onto aerosol particles, dry deposition and wet deposition is expected to be insignificant.

The two nonphysical processes that are expected to be most significant in the removal of dimethylphenols from aquatic media are their reactions with peroxy radicals and biodegradation. From the estimated rate constant for 2,4-dimethylphenol reaction with peroxy radicals (Mabey et al., 1981), it has been estimated that the half-life for this reaction will be <1 day. There is some controversy regarding the significance of biodegradation in determining the fate of dimethylphenols in aquatic media. Biodegradation was found to be significant in natural water by some authors (Visser et al., 1977; Southworth et al., 1985), while Kaplin et al. (1968) reported that significant biodegradation of dimethylphenols is not likely. Based on the estimated biodegradation rate constant value given by Mabey et al. (1981), it is estimated that the biodegradation half-lives of dimethylphenols in natural water will be ~3 days. The loss of dimethylphenols from natural aquatic media through volatilization is likely to be insignificant. The significance of the removal of these compounds through sorption onto suspended particles and sediments will depend on the nature of the particle.

Sorption may become significant when the iron oxide or organic carbon content of the particles in aquatic media is high. Dimethylphenols are not expected to significantly bioconcentrate in aquatic organisms (Barrows et al., 1980; Davies and Dobbs, 1984).

The two processes that may determine the fate of dimethylphenols in soil are biodegradation and sorption (Humenick et al., 1982). Biodegradation, however, was found to be insignificant in the soil from a creosote waste disposal site (Goerlitz et al., 1985). The toxicity of chemicals towards the microorganisms may be responsible for the observed lack of biodegradability at this site. The sorption of dimethylphenols in soil will increase as the organic carbon and iron oxide content of the soil increases (Artiola-Fortuny and Fuller, 1982; Isaacson and Sawhney, 1984). Dimethylphenols may leach into groundwater because of the low sorption in sand aquifers (Goerlitz, et al., 1985). Should the number of microorganisms capable of degrading dimethylphenols decline, because of the presence of toxicants, then leaching would become the primary fate process in soil.

3. EXPOSURE

3.1. AIR

The two most obvious sources of dimethylphenols in the atmosphere are its production and user sites. All the isomers of dimethylphenol except 3,5-diemthylphenol have been identified in cigarette smoke (Kuwata et al., 1981; Arrendale et al., 1982; Hoffmann et al., 1975). The concentration of 2,4- and 2,5-dimethylphenol was reported to be 14.4 μg in the mainstream smoke of 85 mm tobacco cigarettes (Hoffman et al., 1975). 2,4- and 2,5-Dimethylphenol have also been identified in marijuana, at a total concentration of 6.5 μg in the mainstream smoke of a 85 mm cigarette (Hoffmann et al., 1975). All the isomers of dimethylphenol have been identified in diesel and gasoline vehicular exhausts (Mulawa and Cadle, 1981; Hampton et al., 1982; Roumeliotis et al., 1981). 2,6-Dimethylphenol at a concentration of 1.3 ppb was detected in exhaust gas from a metal paint dryer that used the chemical as a solvent (Hoshika et al., 1981a,b). Concentrations of 2,4-, 2,6- and 3,5-dimethylphenols in the indoor air samples of an oil shale wastewater facility were reported to be 6, 2 and 6 $\mu g/m^3$, respectively (Hawthorne and Sievers, 1984). Corresponding concentrations in the outdoor air of the same facility were 1, 0.4 and 1 $\mu g/m^3$ (Hawthorne and Sievers, 1984). 2,6-Dimethylphenol was also identified in henhouse dust samples (Hartung and Rokicki, 1984). Combustion and pyrolysis of building materials containing phenolic resins and foam insulation will produce 2,4- and 2,6-dimethylphenols in the atmosphere (U.S. EPA, 1980).

Although dimethylphenols have been identified from the above mobile and stationary sources, very few studies are available that measure the levels of these compounds in ambient atmosphere. Hawthorne and Sievers (1984) reported the measurements of dimethylphenols in ambient U.S. urban and rural

air. At a detection limit of 0.05 μg/m³, dimethylphenols were not detected in either rural or urban air.

3.2. WATER

The obvious sources of dimethylphenols in surface and groundwater are the coal tar fractionation and coal processing operations, and the user sites of these chemicals. The gross estimate of the U.S. annual discharge of 2,4-dimethylphenol was estimated to be 100 tons (U.S. EPA, 1980). Small quantities of dimethylphenols are also formed during sewage treatment and during the treatment of municipal and industrial wastes. Leachates from municipal and industrial dumpsites may contain dimethylphenols (U.S. EPA, 1980). For example, 2,3-, 2,4-, 2,5- and 3,4-dimethylphenols have been identified in primary effluents from the Los Angeles County Treatment Plant (Young et al., 1983; Gossett et al., 1983; Young, 1978). The concentrations of 2,3- and 2,4-dimethylphenol in the primary effluent were 40 and 14 μg/ℓ, respectively (Gossett et al., 1983; Young et al., 1983). However, the concentration of 2,4-dimethylphenol was reduced to 5 μg/ℓ in the final effluent (Young, 1978; Young et al., 1983). Baird et al. (1977) reported the detection of all six isomers of dimethylphenols in petroleum industry discharges. A concentration as high as 8177 mg/ℓ of 2,3-dimethylphenol was reported in one such discharge (Baird et al., 1977). Pfeffer (1979) reported the detection of 18.3 mg/ℓ of 2,4-dimethylphenol in the separation of a treatment process for petroleum refinery wastewater. 2,4-Dimethylphenol was detected in the secondary effluents from textile plant wastewater at a concentration of 8-9 mg/ℓ (Rawlings and Samfield, 1979). Wastewaters from coal gasification and oil shale treatment facilities have been reported to contain dimethylphenols. For example, 2,3-, 2,4-, 2,6-, 3,4- and 3,5-dimethylphenols were identified in synthane process

water. The combined concentrations of m- and p-cresols and 2,4- and 2,5-dimethylphenol in the process water was 1626 mg/ℓ (Neufeld and Spinola, 1978). Wastewaters from coal liquefaction processes will also contain dimethylphenols as the SRC oil contain all six isomers of dimethylphenols (White and Li, 1982; Dong and DiCesare, 1982). Similarly, wastewaters from shale oil production facilities contain dimethylphenols (Hawthorne and Sievers, 1984). The U.S. EPA's STORET data base contains data on the level of 2,4-dimethylphenols in effluent samples and ambient waters. Using the more reliable data available in STORET data base since the 1980s, Staples et al. (1985) reported concentrations of 2,4-dimethylphenol in effluent and ambient water samples (Table 3-1).

Callahan et al. (1979) monitored several samples collected from residential and industrial wastewaters for the identification of 2,4-dimethylphenol and reported the detection of the compound in 38% of the industrial samples (n=42) at an average concentration of 7 µg/ℓ. This isomer was detected only in 6% of residential samples (n=47). 2,4-Dimethylphenol was also identified in urban runoff water at a frequency of 2% and at an average concentration of 10 µg/ℓ (Cole et al., 1984).

Dimethylphenols have also been detected in underground water near industrial operations or near waste dumpsites. At a well near an underground coal gasification site, Stuermer et al. (1982) reported a concentration of 3,4-dimethylphenol at 780 µg/ℓ. Several investigators identified dimethylphenols in groundwaters near waste dumpsites, particularly from paint factories, wood-preserving facilities, coal tar and wood treating plants and from dumpsites in the Love Canal area (Hauser and Bromberg, 1982; McCreary et al., 1983; Rostad et al., 1984; Botta et al., 1984). Well water located near the center of a site contaminated by coal tar distillate and

TABLE 3-1

Concentration of 2,4-Dimethylphenol in Effluents and Ambient Water*

Sample	No. of Samples	Median Concentration (µg/ℓ)	% Detectable
Effluent	1304	<10	2
Ambient water	813	<10	0.1

*Source: Staples et al., 1985

wood-treating wastes contained several isomers of dimethylphenols (Godsy et al., 1983). The concentrations of 2,5- and 3,5-dimethylphenol in this groundwater were reported to be 5.44 and 6.18 mg/ℓ. Goerlitz et al. (1985) also reported the detection of all six isomers of dimethylphenol in groundwater from a dumpsite of a wood-preserving facility in Florida. The maximum concentrations of 2,4-and 3,5-dimethylphenol were found to be 5.65 and 9.52 mg/ℓ, respectively at a depth of 6 m.

Although Shackelford and Keith (1976) reported the presence of 2,4-dimethylphenol in fresh drinking water in the United States, the level of the compound was not reported. No other investigation reporting the detection of dimethylphenols in drinking water was found. Callahan et al. (1979) analyzeo a total of six tapwaters from two U.S. cities and failed to detect 2,4-dimethylphenol in any of these waters.

3.3. FOOD

Dimethylphenols have been identified as natural constituents in tea, tobacco, marijuana and conifers (U.S. EPA, 1980). With the exception of 2,4-dimethylphenol, Yajima et al. (1981) identified all the five other isomers of dimethylphenol in the volatile flavor components of dried Bonito (Katsuobushi), a traditional flavor-enhancer used in Japanese foods. Exposure to the dimethylphenols from contaminated edible aquatic organisms is also possible, but the concentrations of these compounds in polluted aquatic organisms are expected to be low because of their low bioaccumulation potential (see Section 2.2.).

3.4. SUMMARY

Although dimethylphenols have been identified in tobacco and marijuana smoke, exhaust from mobile and stationary sources, these compounds have

never been reported to be present in ambient air. Hawthorne and Sievers (1984) failed to detect dimethylphenol in U.S. urban and rural air at a detection limit of 0.05 μg/m³ for the individual compounds.

Dimethylphenols have been identified in the effluents from municipal wastewater treatment plants, petroleum industry discharges, secondary effluents from textile plants, effluents from coal liquefaction and gasification plants and oil shale treatment facilities. Of a total of 1304 effluent samples analyzed, 2% of the samples had detectable amounts of 2,4-dimethylphenol at a median concentration of <10 μg/ℓ (Staples et al., 1985). Only 0.1% of a total of 813 ambient water samples analyzed contained detectable levels of 2,4-dimethylphenol at a median concentration of <10 μg/ℓ (Staples et al., 1985). Dimethylphenols have been identified in groundwater near industrial operations and near waste dumpsites. The concentrations of 2,4- and 3,5-dimethylphenol at a depth of 6 m inside a wood preserving dumpsite in Florida were reported to be 5.65 mg/ℓ and 9.52 mg/ℓ, respectively (Goerlitz et al,. 1985). With the exception one reported instance (Shackelford and Keith, 1976), no isomer of diemthylphenol has ever been detected in U.S. drinking water.

Although dimethylphenols may be present in trace amounts in tea, and in edible aquatic organisms from polluted waters, the quantitative level of the dimethylphenol in any food could not be located in the available literature as cited in the Appendix.

4. PHARMACOKINETICS

Limited information regarding the absorption, distribution, metabolism and excretion of dimethylphenols was located in the available literature.

4.1. ABSORPTION

When C^{14}-3,4-dimethylphenol (labeled at 4-CH_3) was orally administered at a dose of 35 mg/kg to male Wistar rats, ~93.5% of the radioactivity was excreted in the urine in 24 hours, indicating extensive absorption from the gastrointestinal tract (Miyamoto et al., 1969).

4.2. DISTRIBUTION

In rats receiving a 6-hour constant i.v. infusion or after a bolus i.v. injection, 2,4-dimethylphenol was found to distribute rapidly to the brain, liver and fat with ratios to plasma of 3, 1.5 and 2, respectively (Somani et al., 1981; Kaka et al., 1982). The concentration in fat, liver and plasma were not detectable within 60 minutes after dosing, although it did seem to persist in the brain tissue (Somani et al., 1981).

4.3. METABOLISM

According to Kaka et al. (1982), the 2,4-isomer was rapidly metabolized to its conjugates of which the glucuronide accounts for 53% and other conjugates 41%.

4.4. EXCRETION

Rats treated orally with ^{14}C-3,4-dimethylphenol excreted ~93.5% of the radioactivity in the urine collected for 24 hours after dosing (Miyamoto et al., 1969). The content of unchanged 3,4-dimethylphenol was ~5.8% of the urinary radioactivity. Other excretory metabolites identified were 3,4-dimethylphenol sulfate and 3,4-dimethylphenol glucuronide, but these metabolites accounted for >5% of the urinary radioactivity (Miyamoto et al., 1969).

4.5. SUMMARY

From the limited information available on 2,4- and 3,4-dimethylphenol, it appears that the dimethylphenols are extensively and rapidly absorbed from the gastrointestinal tract of rats (Miyamoto et al., 1969) rapidly distributed and eliminated from tissues and rapidly metabolized to glucuronide and sulfate conjugates (Somani et al., 1981; Kaka et al., 1982). Urinary excretion accounted for ~94% of an oral dose in rats (Miyamoto et al., 1969). 2,4-Dimethylphenol tended to persist in the brain of rats after i.v. dosing (Somani et al., 1981).

5. EFFECTS

5.1. CARCINOGENICITY

The ability of dimethylphenol to promote skin tumors in mice following a single initiating dose of DMBA and to act as whole carcinogens on the skin of mice was tested by Boutwell and Bosch (1959). Groups of 30 female Sutter mice (2-3 months of age) were treated with an initial topical application of 75 µg DMBA in benzene, followed by 25 µl of 20% 2,4-, 2,6-, 3,4- or 3,5-dimethylphenol in benzene applied twice weekly to the back of each mouse for 15 weeks. Of the 30 mice in each group, 20-28 survived. Papillomas appeared rapidly in these groups and the response was almost identical to that recorded (50%) for mice when croton oil served as the promotor. 2,6-Dimethylphenol produced the lowest response (30%), while treatment with 3,4-dimethylphenol resulted in 95% of the survivors with papillomas. Only 13% of negative controls (no promotor) had papillomas.

At 15 weeks, 11% of surviving mice treated with 2,4-dimethylphenol had carcinomas; at 23 weeks this incidence was 18%. In mice treated with the 2,6-isomer, 4% had carcinomas at 15 weeks, and 11% had carcinomas at 23 weeks. While no carcinomas were found at 15 weeks in the mice treated with 3,4- and 3,5-dimethylphenol, the incidences at 23 weeks were 14 and 5%, respectively. In the negative and the croton oil controls 0 and 4%, respectively, had carcinomas at 15 weeks and 6 and 8%, respertively had carcinomas at 53 weeks. Therefore, carcinomas appeared in higher incidence and earlier in dimethylphenol-treated mice than in negative and positive controls. In a second experiment, no initiator was used and 25 µl of a 10% solution of the dimethylphenols was applied twice weekly for 20 weeks. The incidences of papillomas in the 2,4-, 2,5-, 3,4- and 3,5-dimethylphenol-treated mice ranged from 24-55%. Mice treated with the 2,6-isomer showed minimal effects

of treatment, and 8% developed papillomas at 20 weeks; none developed carcinomas at 28 weeks. The 3,4- and 3,5-isomer showed the highest response with 50 and 55%, respectively. By week 28, carcinomas developed 8-14% of the mice treated with the other isomers. Results of this study suggest that isomers of dimethylphenol (other than 2,6-) may be carcinogenic to the skin of mice. Pertinent data regarding carcinogenicity of orally administered dimethylphenols could not be located in the available literature as cited in the Appendix.

Kaiser (1967) investigated the ability of black tea to promote skin tumors in groups of 15 Swiss mice after a single initiating application of 1% 3,4-benzopyrene. The tea (1 g brewed for 5 minutes in 155 mL of boiling water) was applied to the neck of the mice on alternate days for 55 applications. No pathological lesions were seen in any of the mice receiving benzopyrene only. Of mice treated with the tea, 6/15 developed epithelial-cell carcinomas in the neck region; all other mice in this group developed precarcinogenic or carcinogenic stages of squamous-cell tumors. Gas chromatographic analysis of the tea revealed that it contained the following compounds: 2,5-, 2,4-, 3,5- and 3,4-isomers of dimethylphenol and o-, m- and p-cresols (Kaiser, 1967).

5.2. MUTAGENICITY

Negative results (Table 5-1) for dimethylphenols were reported in reverse mutation assays when tested in Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation and in Escherichia coli Sd-4-73 (Pool and Lin, 1982; Florin et al., 1980; Szybalski, 1958). Other information regarding the mutagenicity of dimethylphenols could not be located in the available literature as cited in the Appendix.

TABLE 5-1

Mutagenicity Testing of Dimethylphenols

Assay	Indicator/ Organism	Compound and/or Purity	Application	Concentration or Dose	Activating System	Response	Comment	Reference
Reverse mutation	Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100	2,4-dimethyl-phenol/90%	plate incorporation	0, 0.5, 5, 50, 500 and 5000 µg/plate	±S-9	-	NC	Pool and Lin, 1982
Reverse mutation	S. typhimurium TA98, TA100, TA1535, TA1538	2,3-, 2,4-, 2,5-, 2,6-, 3,4-, or 3,5-dimethyl-phenol/purified	spot test	3 µmol/plate	±S-9	-	All negative	Florin et al., 1980
Reverse mutation	S. typhimurium TA98, TA100, TA1535, TA1538	2,4- or 3,5-dimethylphenol/ purified	plate incorporation	0.03, 0.3, 3 or 30 µmol/plate	±S-9	-	Toxic at 30 µmol/plate	Florin et al., 1980
Reverse mutation	Escherichia coli Sd-4-73	2,4-dimethyl-phenol/purity NR	spot test	0.01-0.025 mL	none	-	NC	Szybalski, 1958

NR = Not reported; NC = no comment

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of dimethylphenols could not be located in the available literature as cited in the Appendix.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of dimethylphenols could not be located in the available literature as cited in the Appendix.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Relatively little information was located on the subchronic and chronic toxicity of dimethylphenols. All of the studies located were taken from the Russian literature and only limited details were reported.

Maazik (1967) reported the results of subchronic oral administration of 2,6- and 3,4-dimethylphenol in rats. Groups of 10 male albino rats were treated orally with 29.5 mg/kg/day 2,6-dimethylphenol or 72.5 mg/kg/day 3,4-dimethylphenol for 10 weeks. Another group of 10 rats served as controls. Both groups showed decreased weight gain. The rats treated with 3,4-dimethylphenol had increased weights of the spleen, heart, liver and lungs when compared with the controls. The rats given the 2,6-isomer had increased relative liver and spleen weights. Histological examination showed marked atrophy and parenchymatous dystrophy of the liver cells in both groups. Hematological and clinical chemistry analyses were unremarkable. No other details of the study were reported.

Veldre and Janes (1979) studied the toxicity of Estonian shale oil. Dimethylphenols constitute a large part of the volatile fraction of oil shale wastes. Volatile phenols were administered orally to rats and rabbits for 7 months. The largest dose tested, 38.6 mg/kg/day, resulted in weight loss, elevated blood pressure and parenchymatous dystrophy of the liver, kidneys and spleen. These effects were not observed at 3.86 or 0.386

mg/kg/day. No other details of the study were given. In another experiment, 2,6- or 3,4-dimethylphenol were administered orally to white rats for an 8-month period (Veldre and Janes, 1979). No toxic effects were seen at 0.6 mg/kg/day of 2,6-dimethylphenol and 1.4 mg/kg/day of 3,4-dimethylphenol. At a dose of 6 mg/kg/day of 2,6-dimethylphenol and 14 mg/kg/day of 3,4-dimethylphenol, decreased weight gain and changes in blood pressure and histopathological changes were observed in internal organs (not otherwise specified). Further details of the study were not reported.

Maazik (1967, 1968) reported the results of the same or a similar study; however, the intermediate doses of 0.6 and 1.4 mg/kg/day for the 2,6- and the 3,4-isomers, respectively, were not used. Male albino rats (n=53) were administered 2,6-dimethylphenol in oral doses of 0.06 and 6 mg/kg/day and 3,4-dimethylphenol in doses of 0.14 and 14 mg/kg/day for 8 months. No toxic effects were observed at the 0.06 and 0.14 mg/kg doses (Maazik, 1967, 1968). At doses of 6 mg/kg/day 2,6-dimethylphenol and 14 mg/kg/day 3,4-dimethylphenol, growth rate and blood pressure were reduced compared with controls. Histological changes were observed in the liver, spleen, kidneys and heart of rats fed both isomers; these included fatty dystrophy and atrophy of hepatic cells, hyaline-droplet dystrophy in the kidneys, proliferation of myeloid and reticular cells, atrophy of the lymphoid follicles in the spleen and parenchymatous dystrophy of the heart cells (Maazik, 1967, 1970). No other details of the study were reported.

5.6. OTHER RELEVANT INFORMATION

LD_{50} values for dimethylphenols are presented in Table 5-2. Based on these values, it appears that the order of acute toxicity by the oral route for rats is 2,6- > 2,5- > 3,5- > 3,4- >> 2,4-dimethylphenol and for mice is 2,5- ≈ 3,4- ≈ 3,5- > 2,4- > 2,6-dimethylphenol. Oral LD_{50} values were

TABLE 5-2

LD_{50} Values of Dimethylphenols

Compound	Route	Species	LD_{50} (mg/kg)	Reference
2,4-Dimethylphenol	oral	rat	3200	NIOSH, 1985
	oral	mouse	809	NIOSH, 1985
	skin	rat	1040	NIOSH, 1985
	skin	mouse	1040	NIOSH, 1985
	i.p.	mouse	183	NIOSH, 1985
	i.v.	mouse	100	NIOSH, 1985
2,6-Dimethylphenol	oral	rat	296	Maazik, 1967
	oral	mouse	980	Maazik, 1967
	skin	mouse	920	NIOSH, 1985
	i.p.	mouse	150	NIOSH, 1985
	oral	rabbit	700	Maazik, 1967
	skin	rabbit	1000	NIOSH, 1985
3,4-Dimethylphenol	oral	rat	727	Maazik, 1967
	oral	mouse	400	Maazik, 1967
	oral	rabbit	800	Maazik, 1967
2,5-Dimethylphenol	oral	rat	444	Maazik, 1967
	oral	mouse	383	Maazik, 1967
	oral	rabbit	938	Maazik, 1967
2,3-Dimethylphenol	i.v.	mouse	56	NIOSH, 1985
3,5-Dimethylphenol	oral	rat	608	Maazik, 1967
	oral	mouse	477	Maazik, 1967
	oral	rabbit	1313	Maazik, 1967

not found for 2,3-dimethylphenol. Mice appear to be much more sensitive to 2,4-dimethylphenol and slightly more sensitive to 3,4-, 2,5- and 3,5-dimethylphenol than are rats. Rats are more sensitive to 2,6-dimethylphenol than are mice. Lindgren et al. (1977) reported that 2,6-dimethylphenol was an inhibitor of prostaglandin synthesis in the 3T3 fibroblasts. The isomer was also a potent inhibitor of serotonin release, prostaglandin synthesis and arachidonic acid induced aggregation of human platelets. Because of its inhibitory effect on prostaglandin synthetase, the 2,6-isomer was reported to enhance the natural and antibody-dependent lymphocyte cytotoxicity and thereby affect the tumor target cells by an inhibition of prostaglandin synthesis (Droller et al., 1978).

5.7. SUMMARY

No subchronic or chronic oral carcinogenicity studies have been performed on dimethylphenols. However, data are available to suggest that the 2,4-, 2,5-, 3,4- and 3,5-dimethylphenol isomers exhibit tumor promoting activity on mouse skin (Boutwell and Bosch, 1959). The 2,6-isomer was only weakly effective as a promoting agent. Some of these isomers also may act as whole carcinogens on the skin of mice.

The 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dimethylphenol isomers were found to be nonmutagenic when tested with or without metabolic activation in the TA98, TA100, TA1535, TA1537 and TA1538 strains of Salmonella typhimurium (Pool and Lin, 1982; Florin et al., 1980). The 2,4-isomer was negative in a reverse mutation assay using Escherichia coli Sd-4-73 (Szybalski, 1958).

Pertinent data regarding the teratogenicity and reproductive effects of dimethylphenols could not be located in the available literature as cited in the Appendix.

Studies concerning the chronic toxicity of methylphenols were not located. Limited information, however, was reported on the subchronic oral toxicity of 2,6- and 3,4-dimethylphenol. No toxic effects were noted at 0.6 and 1.4 mg/kg when 2,6- and 3,4-dimethylphenol, respectively, were orally administered to white rats for 8 months (Veldre and Janes, 1979). At doses of 6 and 14 mg/kg (2,6- and 3,4-dimethylphenol) significant changes were noted in blood pressure and body weight, and histopathological changes were noted in the liver, kidney and spleen (Veldre and Janes, 1979; Maazik, 1967, 1970).

6. AQUATIC TOXICITY

6.1. ACUTE

The available information concerning acute toxicity of dimethylphenols is summarized in Table 6-1. Albersmeyer and von Erichsen (1959) compared the toxicity of four isomers (2,4-, 2,5-, 3,4- and 3,5-dimethylphenol) with four fish species (crucian carp, roach, tench and rainbow trout). They concluded that 2,5-dimethylphenol was about twice as toxic as 2,4- and 3,4-dimethylphenol. Studies with fewer isomers and other species indicated that 2,4-dimethylphenol was more toxic than 2,6-dimethylphenol (Phipps et al., 1981) and 3,5-dimethylphenol (Bandt, 1958). In the only study in which a marine species was used, there was little difference in the toxicities of 2,6-, 3,4- and 3,5-dimethylphenol to the shrimp, Crangon franciscorum (McLeese et al., 1979). It is difficult to make further comparisons regarding the relative toxicities of dimethylphenol isomers using data from different studies because of the variability in the LC_{50} values, caused by differences in test conditions. The rest of the data, however, tend to indicate that 2,4-dimethylphenol is also quite toxic, causing toxic effects in bluegills, Lepomis macrochirus, at 3.6 mg/ℓ (U.S. EPA, 1978) and in Daphnia magna at 2.1 mg/ℓ (LeBlanc, 1980). The lowest dimethylphenol concentration that was reported to be toxic was 2 mg/ℓ 2,5-dimethylphenol, which was a 24-hour LC_{50} for rainbow trout embryos (Albersmeyer and von Erichsen, 1959).

6.2. CHRONIC

Holcombe et al. (1982) conducted tests with different lifestages of fathead minnows, Pimephales promelas, exposed to 2,4-dimethylphenol for 32 days. Growth of 28-day-old fish was the most sensitive parameter affected by 2,4-dimethylphenol, and was inhibited at 3.11 mg/ℓ but not 1.97 mg/ℓ.

TABLE 6-1

Acute Toxicity of Dimethylphenols to Aquatic Organisms

Species	Isomer	Concentration (mg/L)	Effect	Reference
		FISH		
Bluegill, *Lepomis macrochirus*	2,4	7.75	96-hour LC_{50}	Buccafusco et al., 1981; U.S. EPA, 1978
	2,4	<3.60	NOEC	U.S. EPA, 1978
Rainbow trout, *Salmo gairdneri*	2,5	3.2-5.6	96-hour LC_{50}	Webb et al., 1976
	2,4	28	24-hour LC_{50}, embryos	Albersmeyer and von Erichsen, 1959
	2,5	2	24-hour LC_{50}, embryos	Albersmeyer and von Erichsen, 1959
	3,4	7	24-hour LC_{50}, embryos	Albersmeyer and von Erichsen, 1959
	3,5	50	24-hour LC_{50}, embryos	Albersmeyer and von Erichsen, 1959
Tench, *Tinca* sp.	2,4	13	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
	2,5	9	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
	3,4	18	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
	3,5	51	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
Roach, *Rutilus rutilis*	2,5	10	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
	3,4	16	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
	3,5	18	3-5 day NOEC	Bandt, 1958
	2,4	8	3-5 day NOEC	Bandt, 1958
Crucian carp, *Carassius carassius*	2,4	30	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
	2,5	10	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
	3,4	21	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
	3,5	53	24-hour LC_{50}	Albersmeyer and von Erichsen, 1959
Goldfish, *Carassius auratus*	3,5	22	96-hour LC_{50}	Bridie et al., 1979b

0777p 05/15/86

TABLE 6-1 (cont.)

Species	Isomer	Concentration (mg/L)	Effect	Reference
			FISH (cont.)	
Bream, Abramis brama	3,5	20	3-5 day NOEC	Bandt, 1958
	2,4	10	3-5 day NOEC	Bandt, 1958
Perch, Perca sp.	3,5	15	3-5 day NOEC	Bandt, 1958
	2,4	8	3-5 day NOEC	Bandt, 1958
Fathead minnow, Pimephales promelas	2,4	9.5	48-hour LC_{50}, static	Phipps et al., 1981
	2,4	17.0	96-hour LC_{50}, flowthrough	Phipps et al., 1981
	2,4	13-14	192-hour LC_{50}, flowthrough	Phipps et al., 1981
	2,6	6.7	48-hour LC_{50}, static	Phipps et al., 1981
	2,6	>27	96-hour LC_{50}, flowthrough	Phipps et al., 1981
	2,6	21-23	192-hour LC_{50}, flowthrough	Phipps et al., 1981
	3,4	14	96-hour LC_{50}	Mattson et al., 1976
			INVERTEBRATES	
Water flea, Daphnia magna	2,4	2.1	48-hour LC_{50}	LeBlanc, 1980
	2,4	1.0	NOEC	LeBlanc, 1980
	2,4	2.37	48-hour EC_{50}, immobilization	Randall and Knopp, 1980
	2,6	11.2	LC_{50}	Kopperman et al., 1974
Shrimp, Crangon septemspinosa	2,6	16.5	96-hour lethal threshold	McLeese et al., 1979
	3,4	13.7	96-hour lethal threshold	McLeese et al., 1979
	3,5	14.5	96-hour lethal threshold	McLeese et al., 1979

0771p
05/08/86

Growth and survival were both affected at 5.13 mg/ℓ. Embryos were more resistant to 2,4-dimethylphenol than larvae or juveniles. Holcombe et al. (1982) concluded that the MATC for 2,4-dimethylphenol was 1.97-3.11 mg/ℓ. U.S. EPA (1980) calculated a chronic value of 2.475 mg/ℓ based on these data.

Similar results were obtained in a fathead minnow embryo-larval test reported in U.S. EPA (1978). The estimated MATC based on the results of this study was 1.5-3.2 mg/ℓ 2,4-dimethylphenol. U.S. EPA (1980) calculated a chronic value of 2.191 mg/ℓ from these data.

6.3. PLANTS

Blackman et al. (1955) compared the toxicity of four dimethylphenol isomers in terms of causing chlorosis in duckweed, Lemna minor. They found that 3,5-dimethylphenol was most toxic and 2,6-dimethylphenol least toxic, with 2,4- and 3,5-dimethylphenol intermediate (Table 6-2). Huang and Gloyna (1968) found that 50 mg/ℓ was a NOEC for inhibition of chlorophyll synthesis in Chlorella pyrenoidosa by 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dimethylphenol. Armstrong et al. (1981) reported that 5 mg/ℓ 2,4-dimethylphenol phosphodiesterase activity in the marine alga, Cyclotella meneghiniana, but the toxicological significance of this finding is unclear. In general, it appears that dimethylphenols are much less toxic to aquatic plants than to aquatic animals.

6.4. RESIDUES

Barrows et al. (1980) conducted a pharmacokinetics study with bluegills exposed to 0.0102 mg/ℓ of 2,4-dimethylphenol for 28 days. The steady state whole body BCF was 150, and the half-time for depuration was 1 day.

TABLE 6-2

Dimethylphenol Concentrations that Cause Chlorosis in Duckweed*

Compound	Concentration (mg/ℓ)
2,4-Dimethylphenol	293
2,5-Dimethylphenol	281
2,6-Dimethylphenol	464
3,5-Dimethylphenol	232

*Source: Blackman et al., 1955

6.5. OTHER RELEVANT INFORMATION

Persson (1984) reported data concerning concentrations of dimethylphenol isomers that would impair the flavor of edible fish tissue. The flavor of roach was reported to be impaired by concentrations of 2,4-, 2,5- or 3,5-dimethylphenol as low as 1.0 mg/ℓ. The lowest concentration of 3,4-dimethylphenol that would impair the flavor of carp was 5.0 mg/ℓ.

6.6. SUMMARY

In terms of acute toxicity to fishes, 2,5-dimethlyphenol appears to be the most toxic of the dimethylphenol isomers, based on the few studies in which different isomers were compared. The 2,4-isomer is also relatively toxic. The lowest acutely toxic dimethylphenol concentration was 2 mg/ℓ 2,5-dimethylphenol, which was a 24-hour LC_{50} for rainbow trout embryos (Albersmeyer and von Erichsen, 1959). The only chronic toxicity data were provided by two fathead minnow embryo-larval tests, both of which indicated toxicity thresholds of 1-3 mg/ℓ (Holcombe et al., 1982; U.S. EPA, 1978). The limited information for aquatic plant species indicated that they were much less sensitive than fish or invertebrates. The only pharmacokinetic information available indicated that 2,4-dimethylphenol was not strongly bioaccumulated by bluegills (28-day BCF=150), and that elimination was rapid ($t_{1/2}$ = 1 day).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

An interim ADI of 0.00044 mg/kg/day 3,4-dimethylphenol based on the subchronic oral NOEL of 0.14 mg/kg/day and an interim ADI of 0.00019 mg/kg/day 2,6-dimethylphenol based on the subchronic oral NOEL of 0.06 mg/kg/day in the studies by Maazik (1967, 1968) in male albino rats have been reported by the U.S. EPA (1986). At doses 100-fold greater than these NOELs, pathological changes in the liver and kidney were observed.

7.2. AQUATIC

U.S. EPA (1980) did not derive ambient water quality criteria for dimethylphenols for the protection of aquatic life. They did note that acute toxicity to freshwater organisms occurred at concentrations as low as 2.12 mg/ℓ and would occur at lower concentrations in species more sensitive than those tested.

Mitrovic (1973), representing the EIFAC Working Party on Water Quality Criteria, proposed the following criteria for dimethylphenols. A criterion of 1.0 mg/ℓ of phenols, cresols and dimethylphenols, singly or in combination, was proposed to protect salmonid fish species. In cases where 2,5-dimethylphenol is a major component of phenolic wastes, the recommended criterion is 0.5 mg/ℓ. To protect "coarse fish," apparently referring to nonsalmonid species, the recommended criterion was 2.0 mg/ℓ. Finally, a criterion of 0.5 mg/ℓ, applying specifically to dimethylphenols, was proposed to prevent tainting of flesh of commercial fish species.

8. RISK ASSESSMENT

The 2,4-, 2,5-, 3,4- and 3,5-dimethylphenol isomers appear to exhibit tumor promoting activity in mouse skin when applied twice weekly for 15-20 weeks. These isomers also appear to act as whole carcinogens on the skin of mice. The 2,6-isomer was only weakly effective as a promoting agent (Boutwell and Bosch, 1959). The 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dimethylphenol isomers were negative for reverse mutation in Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 when tested with or without metabolic activation (Florin et al., 1980; Pool and Lin, 1982). The 2,4-isomer was also negative in Escherichia coli Sd-4-73 (Szybalski, 1958). Pertinent data regarding the teratogenic and reproductive effects of dimethylphenols could not be located in the available literature as cited in the Appendix.

Although the data suggest that several isomers of dimethylphenol promote skin cancer or act as whole carcinogens on the skin of mice, the lack of definitive carcinogenicity studies by a relevant exposure route precludes the derivation of a q_1^*. Interim RfDs (formerly referred to as ADIs) have been reported by the U.S. EPA (1986) for the 2,6- and 3,4-isomers of dimethylphenol. An RfD of 0.00019 mg/kg/day was reported for 2,6-dimethylphenol based on a subchronic oral rat NOEL of 0.06 mg/kg/day (Maazik, 1968) and an uncertainty factor of 320. An RfD of 0.00044 mg/kg/day was reported for 3,4-dimethylphenol based on a subchronic oral rat NOEL of 0.14 mg/kg/day (Maazik, 1968) and an uncertainty factor of 320. In their meeting on January 22, 1986, the U.S. EPA ADI (RfD) Review Committee (U.S. EPA, 1986) verified the NOELs from the study by Maazik (1968). The uncertainty factor,

however, was raised from 320 to 1000, which resulted in ADIs of 6×10^{-5} mg/kg/day for 2,6-dimethylphenol and 1×10^{-4} mg/kg/day for 3,4-dimethylphenol. Subsequent to the meeting of the RfD committee and during the preparation of this document, the study by Veldre and Janes (1979), which gives 10-fold higher NOELs, was located. Veldre and Janes (1979) administered 2,6- or 3,4-dimethylphenol orally to white rats for an 8-month period and reported no effects at 0.6 mg/kg 2,6-dimethylphenol or at 1.4 mg/kg 3,4-dimethylphenol. These doses are intermediate between the low and high doses administered by Maazik (1968). Effects on blood pressure, weight gain and histological changes in the liver, kidneys and spleen were reported at the next higher doses (6 mg/kg for 2,6-dimethylphenol and 14 mg/kg for 3,4-dimethylphenol) by both Veldre and Janes (1979) and Maazik (1968).

Dividing the higher NOELS of 0.6 and 1.4 mg/kg by an uncertainty factor of 1000, provisional RfDs of 0.0006 mg/kg/day of the 2,6-isomer (or 0.042 mg/day for a 70 kg human) and 0.0014 mg/kg/day of the 3,4-isomer (or 0.098 mg/day for a 70 kg human) can be derived. Despite these RfDs being 1 order of magnitude higher than the verified ADIs (RfDs), the data taken from Veldre and Janes (1979) represents a well-designed 8-month study which not only supported the adverse effects (LOAELs) reported by Maazik (1968) but also provided intermediate NOELs not tested by Maazik (1968). Until additional chronic/reproductive toxicity data are available, these RfDs can be considered to provide adequate protection against adverse health effects in humans.

Because of the limited evidence that the dimethylphenols act as promotors or whole carcinogens on the skin of mice (Boutwell and Bosch, 1959), these chemicals were placed in IARC Group 3 and CAG Group C (U.S. EPA, 1984b), which means that there is no evidence of its carcinogenicity in humans.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

No studies of chronic duration in animals were located; however, subchronic oral studies in rats were available for consideration in deriving an RQ for the 2,6- and 3,4-isomers of dimethylphenol (Veldre and Janes, 1979; Maazik, 1967, 1970). These studies were discussed in Chapter 5 and are summarized in Table 9-1. The effects observed with both 2,6- and 3,4-dimethylphenol included weight changes in the rats, changes in blood pressure and histopathological changes in the liver, kidneys and spleen. No details regarding the severity of these effects were given by Veldre and Janes (1979), while Maazik (1967, 1970) reported fatty dystrophy and atrophy of hepatic cells, hyaline droplet dystrophy in the kidneys, atrophy of the lymphoid follicles in the spleen and parenchymatous dystrophy of heart cells. The lowest transformed doses at which these effects were reported were 6 and 14 mg/kg/day for 2,6- and 3,4-dimethylphenol, respectively. Since the same effects were reported for the two isomers at different doses, it is appropriate to calculate a CS and RQ for each isomer (Table 9-2). Multiplying 6 and 14 mg/kg/day by the cube root of the ratio of the rat body weight (assumed to be 0.35 kg) to the reference human body weight (70 kg) and by 70 kg results in equivalent human doses of 71.8 and 167.6 mg/day, respectively. Because the study was subchronic and lacked adequate detail, it is appropriate to divide the equivalent human doses by an uncertainty factor of 10, resulting in chronic MEDs of 7.18 and 16.76 mg/day, respectively (see Table 9-2). The MEDs correspond to an RV_d of 4.2 for the 2,6-isomer and 3.7 for the 3,4-isomer. An RV_e of 5 was used based on the combined effect of histological changes in the liver, kidney and spleen and body weight changes. Multiplying the RV_d by the RV_e results in a CS of

TABLE 9-1

Oral Toxicity Summary for Isomers of Dimethylphenol in Male Albino Rats*

No. at Start	Vehicle/ Physical State	Experimental Dose/Exposure	Transformed Animal Dose (mg/kg/day)	Response	Reference
10	2,6-isomer	29.5 mg/kg/day for 10 weeks	29.5	Decreased weight gain, increased weight of the spleen and liver, atrophy and parenchymatous dystrophy of liver cells.	Maazik, 1967
10	3,4-isomer	72.5 mg/kg/day for 10 weeks	72.5	Decreased weight gain, increased weight of the spleen, heart and lungs; atrophy and parenchymatous dystrophy of liver cells.	Maazik, 1967
NR	2,6-isomer	6 mg/kg/day for 8 months	6	Decreased weight gain, changes in blood pressure, and histopathological changes in liver, kidney and spleen (fatty dystrophy and atrophy of hepatic cells, hyaline-droplet dystrophy in the kidneys, atrophy of the lymphoid follicles in the spleen).	Veldre and Janes, 1979; Maazik, 1967, 1970
NR	3,4-isomer	14 mg/kg/day for 8 months	14	Decreased weight gain, changes in blood pressure, and histopathological changes in liver, kidney and spleen (fatty dystrophy and atrophy of hepatic cells, hyaline-droplet dystrophy in the kidneys, atrophy of the lymphoid follicles in the spleen).	Veldre and Janes, 1979; Maazik, 1967, 1970

*Average weight of rats and purity of compound were not reported

NR = Not reported

TABLE 9-2

Oral Composite Scores for Isomers of Dimethylphenol in the Rat

Isomer	Dose/Exposure (mg/kg/day)	Human MED (mg/day)	RV_d	Effect	RV_e	CS	RQ	Reference
2,6-	6	7.18	4.2	Weight loss, blood pressure increase, pathomorphological changes in liver, kidney and spleen	5	21	100	Veldre and Janes, 1979; Maazik, 1967, 1970
3,4-	14	16.76	3.7	Weight loss, blood pressure increase, pathomorphological changes in liver, kidney and spleen	5	18.5	1000	Veldre and Janes, 1979; Maazik, 1967, 1970

21.1 for the 2,6-isomer, which corresponds to an RQ of 100, and a CS of 18.5 for the 3,4-isomer, which corresponds to an RQ of 1000. Therefore, the study reported by Veldre and Janes (1979) and Maazik (1970) is recommended as the basis of the RQ for the 2,6- and 3,4-isomers of dimethylphenol (Tables 9-3 and 9-4). Data are not sufficient to derive RQs for the other isomers (Table 9-5).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

No subchronic or chronic oral carcinogenicity studies have been reported on dimethylphenols. Data are available, however, to suggest that the 2,4-, 2,5-, 3,4- and 3,5-dimethylphenol isomers exhibit tumor promoting activity on mouse skin (Boutwell and Bosch, 1959). These isomers may also act as whole carcinogens on mouse skin. The data are, however, inadequate to derive an F factor. No data regarding the carcinogenicity of dimethylphenols in humans were located. Therefore, there is limited evidence that dimethylphenols are carcinogenic to animals. Based on the IARC classification scheme, dimethylphenols are Group 3 chemicals, which cannot be classified as to its carcinogenicity for humans. Based on the CAG classification, the dimethylphenols are Group C chemicals (U.S. EPA, 1984).

TABLE 9-3

2,6-Dimethylphenol

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	Oral
Dose*:	7.18 mg/day
Effect:	Decreased weight gain, blood pressure increase, histopathological changes in liver, kidney and spleen
Reference:	Veldre and Janes, 1979; Maazik, 1967, 1970
RV_d:	4.2
RV_e:	5
Composite Score:	21.1
RQ:	100

*Equivalent human dose

TABLE 9-4

3,4-Dimethylphenol

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	Oral
Dose*:	16.76 mg/day
Effect:	Decreased weight gain, blood pressure increase, histopathological changes in liver, kidney and spleen
Reference:	Veldre and Janes, 1979; Maazik, 1967, 1970
RV_d:	3.7
RV_e:	5
Composite Score:	18.5
RQ:	1000

*Equivalent human dose

TABLE 9-5

2,3-, 2,4-, 2,5- and 3,5-Dimethylphenols

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	
Dose:	
Effect:	
Reference:	
RV_d:	
RV_e:	
Composite Score:	
RQ:	Data are not sufficient for deriving an RQ.

Dimethylphenols

10. REFERENCES

Albersmeyer, W. and L. von Erichsen. 1954. Untersuchungen zur Wirung von Teerbestandteilen in Abwassern. Mitteilungen 1-7. Z. Fisch. 8: 29-66. (Cited in Mitrovic, 1973)

Armstrong, J.E., S.W.G. Fehler and J.A. Calder. 1981. Effects of petroleum hydrocarbons on the growth and energetics of marine microalgae. Biol. Monit. Mar. Pollut. Meeting Data, 1979. p. 449-466.

Arrendale, R.F., R.F. Severson, O.T. Chortyk and M.E. Snook. 1982. Analyses of monohydroxybenzenes and dihydroxybenzenes in tobacco smoke and pyrolyzates by glass capillary gas chromatography. J. Chromatogr. Sci. 20(3): 136-143.

Artiola-Fortuny, J. and W.H. Fuller. 1982. Adsorption of some monohydrobenzene derivatives by soils. Soil Sci. 133: 18-26.

Atkinson, R. 1985. Kinetics and mechanisms of the gas phase reactions of the hydroxyl radical with organic compounds under atmospheric conditions, Prepublication copy send to Chem. Rev.

Baird, R.B., L.G. Carmona and R.L. Jenkins. 1977. The direct injection gas liquid chromatography analysis of xylenols in industrial wastewaters. Bull. Environ. Contam. Toxicol. 17(6): 764-767.

Bandt, H.J. 1958. Phenolabwasser and Abwasserphenole, ihre Entstenhung, Schadwirkung und abwassertechnische Behandlung. Eine monographische Studie. Wiss. Abhandlg., 33 Berlin, Academia Berlag. 36 p. (Cited in Mitrovic, 1973)

Banerjee, S., S.H. Yalkowsky and S.C. Valvani. 1980. Water solubility and octanol/water partition coefficients of organic limitations of the solubility partition coefficient correlation. Environ. Sci. Technol. 11: 1227-1229.

Barrows, M.E., S.R. Petrocelli, K.J. Macek and J.J. Carroll. 1980. Bioconcentration and elimination of selected water pollutants by the bluegill sunfish, Lepomis macrochirus. Dyn. Exposure Hazard Assess. Toxic Chem. p. 379-392.

Blackman, G.E., M.H. Parke and G. Garton. 1955. The physiological activity of substituted phenols. I. Relationships between chemical structure and physiological activity. Arch. Biochem. Biophysics. 54: 45-54.

Botta, D., P.L. Castellani and E. Mantica. 1984. Groundwater pollution by organic solvents and their microbial degradation products. Comm. Eur. Commun. 8518: 261-275.

Boutwell, R.K. and D.K. Bosch. 1959. The tumor-promoting action of phenol and related compounds for mouse skin. Cancer Res. 19: 413-424.

Bridie, A.L., C.J.M. Wolff and M. Winter. 1979a. BOD and COD of some petrochemicals. Water Res. 13(7): 627-630.

Bridie, A.L., C.J.M. Wolff and M. Winter. 1979b. The acute toxicity of some petrochemicals to goldfish. Water Res. 13(7): 623-626.

Buccafusco, R.J., S.J. Ells and G.A. LeBlanc. 1981. Acute toxicity of priority pollutants to bluegill, Lepomis macrochirus. Bull. Environ. Contam. Toxicol. 26(4): 446-452.

Callahan, M.A., D.J. Ehreth and P.L. Levins. 1979. Sources of toxic pollutants found in influent to sewage treatment plants. Proc. Natl. Conf. Munic. Sludge Manage. 8: 55-61.

Carter, W.P.L., A.M. Winer and J.N. Pitts, Jr. 1981. Major atmospheric sink for phenol and the cresols. Reaction with the nitrate radical. Environ. Sci. Technol. 15: 829-831.

CASR (Chemical Activities Status Report). 1985. Online: October 1985

Chambers, C.W., H.H. Tabak and P.W. Kabler. 1963. Degradation of aromatic compounds by phenol-adapted bacteria. J. Water Pollut. Control Fed. 35: 1517-1528.

Chao, J., C.T. Lin and T.H. Chung. 1983. Vapor pressure of coal chemicals. J. Phys. Chem. Ref. Data. 12: 1033-1063.

Chapman, P.J. and D.J. Hopper. 1968. Bacterial metabolism of 2,4-xylenol. Biochem. J. 110(3): 491-498.

Cole, R.H., R.E. Frederick, R.P. Healy and R.G. Rolan. 1984. Preliminary findings of the priority pollutant monitoring project of the nationwide urban runoff program. J. Water Pollut. Control Fed. 56(7): 898-908.

Cupitt, L.T. 1980. Fate of toxic and hazardous materials in the air environment. Environmental Sciences Research Laboratory, Office of Research and Development, U.S. EPA, Research Triangle Park, NC. EPA-600/3-80-084. NTIS-PB-80-221948.

Davies, R.P. and A.J. Dobbs. 1984. The prediction of bioconcentration in fish. Water Res. 18(10): 1253-1262.

Dong, M.W. and J.L. DiCesare. 1982. Analysis of priority pollutants by very high-speed LC. J. Chromatogr. Sci. 20(11): 517-522.

Dourson, M.L. 1986. U.S. EPA, Cincinnati, OH. Telephone conversation with S. Wilbur, Syracuse Research Corp., Syracuse, NY. April 28.

Droller, M.J., P. Perlmann and M.U. Schneider. 1978. Enhancement of natural and antibody-dependent lymphocyte cytotoxicity by drugs which inhibit prostaglandin production by tumor target cells. Cell. Immunol. 39(1): 154-164.

Dunn, G.F., Jr. and D.G. Hutton. 1983. The combined powdered activated carbon-activated sludge (PACT) process for toxics control. Water Resour. Symp. 10: 53-76.

Fedorak, P.M. and S.E. Hrudey. 1984. The effects of phenol and some alkyl phenolics on batch anaerobic methanogenesis. Water Res. 18(3): 361-368.

Florin, I., L. Rutberg, M. Curvall and C.R. Enzell. 1980. Screening of tobacco smoke constituents for mutagenicity using the Ames' test. Toxicology. 15(3): 219-232.

Fujita, T. and M. Nakajima. 1969. The correlation between physiological activity and physicochemical property of the substituted phenols. Res. Rev. 25: 319-326.

Garst, J.E. and W.C. Wilson. 1984. Accurate, wide-range, automated, high-performance liquid chromatographic method for the estimation of octanol/water partition coefficients. I: Effect of chromatographic conditions and procedure variables on accuracy and reproducibility of the method. J. Pharm. Sci. 73(11): 1616-1623.

Godsy, E.M., D.F. Goerlitz and G.G. Ehrlich. 1983. Methanogenesis of phenolic compounds by a bacterial consortium from a contaminated aquifer in St. Louis Park, Minnesota. Bull. Environ. Contam. Toxicol. 30(3): 261-268.

Goerlitz, D.F., D.E. Troutman, E.M. Godsy and B.J. Franks. 1985. Migration of wood-preserving chemicals in contaminated groundwater in a sand aquifer at Pensacola, FL. Environ. Sci. Technol. 19(10): 955-961.

Gossett, R.W., D.A. Brown and D.R. Young. 1983. Predicting the bioaccumulation of organic compounds in marine organisms using octanol/water partition coefficients. Mar. Pollut. Bull. 14(10): 387-392.

Hampton, C.V., W.R. Pierson, T.M. Harvey, N.S. Updegraove and R.S. Marano. 1982. Hydrocarbon gases emitted from vehicles on the road. I. A qualitative gas chromatography/mass spectrometry survey. Environ. Sci. Technol. 16: 287-298.

Hansch, C. and A.J. Leo. 1981. Medchem. Project. Issue No. 19. Pomona College, Claremont, CA.

Hartung, J. and E. Rokicki. 1984. Occurrence of phenolic compounds in the dust of swine stalls and henhouses. Zentralbl Bakteriol Mikrobiol Hyg. 179: 431-439.

Hauser, T.R. and S.M. Bromberg. 1982. Environmental Protection Agency monitoring program at Love Canal, New York 1980. Environ. Monit. Assess. 2(3): 249-272.

Hawley, G.G. 1981. The Condensed Chemical Dictionary, 10th ed. Van Nostrand Reinhold Co., New York. p. 1101.

Hawthorne, S.B. and R.E. Sievers. 1984. Emission of organic air pollutants from shale oil wastewaters. Environ. Sci. Technol. 18(6): 483-490.

Hawthorne, S.B., R.E. Sievers and R.M. Barkley. 1985. Organic emissions from shale oil wastewaters and their implications for air quality. Environ. Sci. Technol. 19(10): 992-997.

Hoffmann, D., K.D. Brunnemann, G.B. Gori and E.L. Wynder. 1975. On the carcinogenicity of marijuana smoke. Recent Adv. Phytochem. 9: 63-81.

Holcombe, G.W., G.L. Phipps and J.T. Fiandt. 1982. Effects of phenol, 2,4-dimethylphenol, 2,4-dichlorophenol and pentachlorophenol on embryo, larval and juvenile fathead minnows, Pimephales promelas. Arch. Environ. Contam. Toxicol. 11(1): 73-78.

Hopper, D.J. and P.J. Chapman. 1971. Gentisic acid and its 3- and 4-methyl-substituted homologs as intermediates in the bacterial degradation of m-cresol, 3,5-xylenol and 2,5-xylenol. Biochem. J. 122(1): 19-28.

Hoshika, Y., Y. Nihei and G. Muto. 1981a. Pattern display for characterization of trace amounts of odorants discharged from nine odor sources. Analyst. 106: 1187-1202.

Hoshika, Y., Y. Nihei and G. Muto. 1981b. Simple circular odor chart for characterization of trace amounts of odorants discharged from thirteen odor sources. J. Chromatogr. Sci. 19(4): 200-215.

Huang, J.C. and E.F. Gloyna. 1968. Effect of organic compounds on photosynthetic oxygenation. I. Chlorophyll destruction and suppression of photosynthetic oxygen production. Water Res. 2: 347-366.

Heukelekian, H. and M.C. Rand. 1955. Biochemical oxygen demand of pure organic compounds. J. Water Pollut. Control Assoc. 29: 1040-1053.

Humenick, M.J., L.N. Britton and C.F. Mattox. 1982. Natural restoration of groundwater in UCG. In Situ. 6: 107-125.

Isaacson, P.J. and B.L. Sawhney. 1984. Measurement of vapor sorption: Influence of organic matter on clay sorption of 2,6-dimethylphenol. Soil Sci. 138(6): 436-439.

Kaiser, H.E. 1967. Cancer-promoting effects of phenols in tea. Cancer. 20(5): 614-616.

Kaka, J.S., S.M. Somani and D.J. Schaeffer. 1982. Metabolism and distribution of 2,4-dimethylphenol in rat. Ecotoxicol. Environ. Saf. 6(1): 35-40. (CA 96:175498c)

Kaplin, V.T., L.V. Semenchenko and E.G. Ivanov. 1968. Decomposition of a phenol mixture in natural waters (miniature-scale operation). Gidrokhim. Mater. 46: 199-202.

Kitano, M. 1978. Biodegradation and bioaccumulation test on chemical substances. OECD Conference, Tokyo. Reference Book TSU-No. 3.

Kopperman, H.L., R.M. Carlson and R. Caple. 1974. Aqueous chlorination and ozonation studies. I. Structure-toxicity correlations of phenolic compounds to Daphnia magna. Chem. Biol. Interact. 9(4): 245-251.

Kuwata, K., M. Uebori and Y. Yamazaki. 1981. Reversed-phase liquid chromatographic determination of phenols in auto exhaust and tobacco smoke as p-nitrobenzeneazophenol derivatives. Anal. Chem. 53(9): 1531-1534.

LeBlanc, G.A. 1980. Acute toxicity of priority pollutants to water flea, Daphnia magna. Bull. Environ. Contam. Toxicol. 24(5): 684-691.

Lindgren, B.O. and B. Ericsson. 1969. Reaction of chlorine dioxide with phenols: Formation of α,β-epoxy ketones from mesitol and 2,6-xylenol. Acta Chem. Scandinav. 23: 3451-3460.

Lindgren, J.A., H.E. Claesson and S. Hammarstrom. 1977. Inhibition of prostaglandin synthesis in mouse 3T3 fibroblasts and human platelets by substituting phenols. Prostaglandins. 13: 1093-1102.

Lyman, W.J., W.F. Reehl and D.H. Rosenblatt. 1982. Handbook of Chemical Property Estimation Methods. Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York. p. 4-9, 15-16, 10-27.

Maazik, I.K. 1967. Standards for dimethylphenol isomers in water bodies. Gig. Sanit. (Hygiene and Sanitation). 11: 28-35. (In Russian with English translation)

Maazik, I. 1968. Dimethylphenol (xylenol) isomers and their standard contents in water reservoirs. Gig. Sanit. 33(9): 18-22. (Russ.) (CA 69:109642m)

Maazik, I. 1970. Toxicity of small dimethylphenol doses in chronic experiments. Vop. Gig. Tr. Prof. Patol. Est. SSR. 2: 171-176. (Russ.) (CA 74:51747j)

Mabey, W.R., J.H. Smith, R.T. Podoll, et al. 1981. Aquatic Fate Process Data for organic Priority Pollutants. Monitoring and Data Support Div., Office of Water Regulations and Standards, Washington, DC. EPA 440/4-81-014.

Mattson, V.R., J.W. Arthur and C.T. Wallbridge. 1976. Acute toxicity of selected organic compounds to fathead minnows. U.S. EPA, Office of Research and Development, Washington, DC. EPA 600/3-76-097. p. 13.

McCreary, J.J., J.G. Jackson and J. Zoltek, Jr. 1983. Toxic chemicals in an abandoned phenolic waste site. Chemosphere. 12(11-12): 1619-1632.

McLeese, D.W., V. Zitko and M.R. Peterson. 1979. Structure-lethality relationships for phenols, anilines and other aromatic compounds in shrimp and clams. Chemosphere. 8(2): 53-57.

Mill, T., W.R. Mabey and D.G. Hendry. 1980. Oxidation in water. In: Laboratory Protocols for Evaluating the Fate of Organic Chemicals in Air and Water, T. Mill and D.G. Hendry, Ed. ERL, ORD, Athens, GA. EPA 68-03-2227. p. 103-138.

Mitrovic, V. 1973. Water quality criteria for European freshwater fish. Water Research. 7: 929-941.

Miyamoto, J., K. Yamamoto and T. Matsumoto. 1969. Metabolism of 3,4-dimethylpehnyl-N-methylcaramate in white rats. Agr. Biol. Chem. 33(7): 1060-1073.

Mulawa, P.A. and S.H. Cadle. 1981. Measurement of phenols in automobile exhaust. Anal. Lett. 14: 671-688.

Neufeld, R.D. and A.A. Spinola. 1978. Ozonation of coal gasification plant wastewater. Environ. Sci. Technol. 12(4): 470-472.

NIOSH (National Institute for Occupational Safety and Health). 1985. RTECS (Registry of Toxic Effects of Chemical Substance) Online, October, 1985.

OHMTADS (Oil and Hazardous Materials Technical Assistance Data Systems). 1985. On-line: October, 1985.

Papa, A.J. and P.D. Sherman, Jr. 1981. Ketones. In: Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 13, 3rd ed., M. Grayson, Ed. John Wiley and Sons, New York. p. 920.

Patterson, J.W. and P.S. Kodukala. 1981. Biodegradation of hazardous organic pollutants. Chem. Eng. Prog. 77: 48-55.

Pearce, P.J. and R.J.J. Simkins. 1968. Acid strengths of some substituted picric acids. Can. J. Chem. 46: 241-248.

Persson, P.E. 1984. Uptake and release of environmentally occurring odorous compounds by fish a review. Water Res. 18(10): 1263-1272.

Petrasek, A.C., I.J. Kugelman and B.M. Austern. 1983. Fate of toxic organic compounds in wastewater treatment plants. J. Water Pollut. Control Fed. 55(10): 1286-1296.

Pfeffer, F.M. 1979. The 1977 screening survey for measurement of organic priority pollutants in petroleum refinery wastewaters. ASTM Spec. Tech. Publ. 686: 181-190.

Phipps, G.L., G.W. Holcombe and J.T. Fiandt. 1981. Acute toxicity of phenol and substituted phenols to the fathead minnow. Bull. Environ. Contam. Toxicol. 26(5): 585-593.

Pitter, P. 1976. Determination of biological degradability of organic substances. Water Res. 10(3): 231-235.

Pitter, P. and P. Kucharova-Rosolova. 1974. Relation between the structure and biodegradability of organic compounds. III. Biodegradability of aromatic hydroxy derivatives. Sb. Vys. Sk. Chem.-Technol. Praze, Technol. Vody. 49: 43-57.

Poh, C.L. and R.C. Bayly. 1980. Evidence for isofunctional enzymes used in m-cresol and 2,5-xylenol degradation via the gentisate pathway in Pseudomonas alcaligenes. J. Bacteriol. 143(1): 59-69.

Pool, B.L. and P.Z. Lin. 1982. Mutagenicity testing in the Salmonella typhimurium assay of phenolic compounds and phenolic fractions obtained from smokehouse smoke condensates. Food Chem. Toxicol. 20(4): 383-391.

Randall, T.L. and P.V. Knopp. 1980. Detoxification of specific organic substances by wet oxidation. J. Water Pollut. Control Fed. 52(8): 2117-2130.

Rawlings, G.D. and M. Samfield. 1979. Toxicity of secondary effluents from textile plants. Office of Research and Development, U.S. EPA. EPA 600/7-78-168. PB-290. 331: 153-169.

Reed, H.W.B. 1978. Alkylation. In: Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 2, 3rd ed., M. Grayson, Ed. John Wiley and Sons, New York. p. 66.

Rogers, J.A. 1982. Solution thermodynamics of phenols. Int. J. Pharmaceut. 10: 89-97.

Rostad, C.E., W.E. Pereira and S.M. Ratcliff. 1984. Bonded-phase extraction column isolation of organic compounds in groundwater at a hazardous waste site. Anal. Chem. 56(14): 2856-2860.

Roumeliotis, P., W. Liebald and K.K. Unger. 1981. Determination of phenols from automobile exhaust by means of high-performance liquid chromatography. Int. J. Environ. Anal. Chem. 9(1): 27-44.

Sadtler, B. n.d. Sadtler Standard Spectra. Sadtler Research Lab., Philadelphia, PA.

Shackelford, W.M. and L.H. Keith. 1976. Frequency of organic compounds identified in water. Environmental Research Laboratory Office of Research and Development, U.S. EPA, Athens, GA. EPA 600/4-76-062. 238 p.

Somani, S.M., J.S. Kaka and T.A. Smart. 1981. Disposition of 2,4-dimethylphenol and 2,4-dichlorophenol in rat. 65th Annual Meeting of the Federation of American Societies for Experimental Biology, Atlanta, GA. April 12-17, 1981. Fed. Proc. 40: 698.

Southworth, G.R., S.E. Herbes, P.J. Franco and J.M. Giddings. 1985. Persistence of phenols in aquatic microcosms receiving chronic inputs of coal-derived oil. Water Air Soil Pollut. 24(3): 283-296.

SRI (Stanford Research Institute). 1985. Directory of Chemical Producers. United States of America. SRI International, Menlo Park, CA. p. 963.

Staples, C.A., A. Werner and T. Hoogheem. 1985. Assessment of priority pollutant concentrations in the United States using STORET Database. Environ. Toxicol. Chem. 4: 131-142.

Stuermer, D.H., D.J. Ng and C.J. Morris. 1982. Organic contaminants in groundwater near an underground coal gasification site in northeastern Wyoming. Environ. Sci. Technol. 16(9): 582-587.

Szybalski, W. 1958. Special microbiological systems. 2. Observations on chemical mutagenesis in microorganisms. Ann. NY Acad. Sci. 76: 475-489.

Tabak, H.H., C.W. Chambers and P.W. Kabler. 1964. Microbial metabolism of aromatic compounds. I. Decomposition of phenolic compounds and aromatic hydrocarbons by phenol-adapted bacteria. J. Bacteriol. 87: 910-919.

Tabak, H.H., S.A. Quave, C.I. Mashni and E.F. Barth. 1981. Biodegradability studies with organic priority pollutant compounds. J. Water Pollut. Control Fed. 53(10): 1503-1518.

U.S. EPA. 1977. Computer print-out of non-confidential production data from TSCA inventory. OPTS, CID, U.S. EPA, Washington, DC.

U.S. EPA. 1978. In-depth studies on health and environmental impacts of selected water pollutants. Prepared by EG&G Bionomics, Wareham, MA under Contract No. 68-01-4646.

U.S. EPA. 1980. Ambient Water Quality Criteria for 2,4-Dimethylphenol. Office of Water Regulations and Standards, Criteria and Standards Div., Washington, DC. EPA 440/5-80-044. NTIS PB81-117558.

U.S. EPA. 1984. Proposed Guidelines for Carcinogen Risk Assessment. Federal Register. 49(227): 46294-46301.

U.S. EPA. 1986. Meeting Notes from RfD Committee. January 22, 1986.

USITC (U.S. International Trade Commission). 1985. Synthetic Organic Chemicals. U.S. Production and Sales, 1984. USITC Publ. No. 1745, Washington, DC. p. 48.

Veldre, I.A. and H.J. Janes. 1979. Toxicological studies of shale oils, some of their components and commercial products. Environ. Health Perspect. 30: 141-146.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., New York. p. 1195-1198.

Visser, S.A., G. Lamontagne, V. Zoulalian and A. Tessier. 1977. Bacteria active in the degradation of phenols in polluted waters of the St. Lawrence River. Arch. Environ. Contam. Toxicol. 6(4): 455-469.

Weast, R.C., Ed. 1980. CRC Handbook of Chemistry and Physics, 61st ed. CRC Press, Inc., Boca Raton, FL. p. C476-C478.

Webb, M., H. Ruber and G. Leduc. 1976. The toxicity of various mining flotation reagents to rainbow trout, Salmo gairdneri. Water Res. 10(4): 303-306.

Weber, R.C., P.A. Parker and M. Bowser. 1981. Vapor pressure distribution of selected organic chemicals. U.S. EPA, Cincinnati, OH. p. 34. EPA 600/2-81-021.

Westall, J.C., C. Leuenberger and R.P. Schwarzenbach. 1985. Influence of pH and ionic strength on the aqueous-nonaqueous distribution of chlorinated phenols. Environ. Sci. Technol. 19(2): 193-198.

White, C.M. and N.C. Li. 1982. Determination of phenols in a coal liquifaction product by gas chromatography and combined gas chromatography-mass spectrometry. Anal. Chem. 54(9): 1570-1572.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ. p. 1448.

Yajima, I., M. Nakamura, H. Sakakibara, T. Yanai and K. Hayashi. 1981. Volatile flavor components of dried bonito. I. On basic, acidic and weak acidic fractions. Agric. Biol. Chem. 45(12): 2761-2768.

Young, D.R. 1978. Priority pollutants in municipal wastewaters. Annu. Rep. - South. Calif. Coastal Water Res. Proj. 103-112.

Young, D.R., R.W. Gossett, R.B. Baird, D.A. Brown, P.A. Taylor and M.J. Mille. 1983. Wastewater inputs and marine bioaccumulation of priority pollutant organics off southern California. Water Chlorination: Environ. Impact Health Eff. 4: 871-884.

APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

CASR online (U.S. EPA Chemical Activities Status Report)
CAS online STN International
TOXLINE
TOXBACK 76
TOXBACK 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP
NTIS
Federal Register

These searches were conducted in October, 1985. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981, 1982, 1983). Cincinnati, OH. 486 p.

ACGIH (American Conference of Governmental Industrial Hygienists). 1985. TLVs: Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1985-1986. Cincinnati, OH. 114 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1983. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., Littleton, MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

ITII (International Technical Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. 700 p.

NTP (National Toxicology Program). 1984. Toxicology Research and Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, N.I. 1979. Dangerous Properties of Industrial Materials, 5th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1984. Directory of Chemical Producers. Menlo Park, CA.

U.S. EPA. 1985. Status Report on Rebuttable Presumption Against Registration (RPAR) or Special Review Process. Registration Standards and the Data Call in Programs. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1985. CSB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (U.S. International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982, USITC Publ. 1422, Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under Contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Res. Publ. 137, Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California, State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. Prepared for the U.S. EPA, Washington, DC. PB-269605.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data. Book 1: Toxicology Data. Office of Pesticide Programs, U.S. EPA, Washington, DC. EPA 540/9-79-003. NTIS PB 80-196876.

In addition, a Food Additive Safety Profile, obtained from the U.S. Food and Drug Administration, was consulted.